This is a story about horseshoe crabs, but we’re going to start by talking about a bird, the red knot, because that’s what people noticed first. We’ll get to the crabs (they aren’t really crabs) and how they save lives (so many lives!) and what’s happening in Asia (it’s even worse than what’s happening here) and climate change (of course). But first, the bird.

It was the birders and ornithologists who noticed the severity. The *rufa* red knot, a shorebird with a migration of more than 9,000 miles from one end of the earth to the other, was declining.

When you’re talking about horseshoe crab conservation, most of the time you’re also talking about the red knot, a type of sandpiper with one of the more baffling migration patterns on the planet. Unimpressive and plain to
the untrained eye, in their lifetimes, the birds can fly the equivalence of a trip to the moon and back.

Every year, the birds migrate from Tierra del Fuego to the Canadian Arctic to breed, and for parts of the trip, they fly for days at a time between meals. The red knots, skinny and exhausted from the first leg of their migration, make a stop at the Delaware Bay just in time for the horseshoe crab spawn in May and June. The birds feast on the tiny, pinhead-sized horseshoe crab eggs for two weeks, doubling their body weight and enabling them to make their way to the Arctic. The trip hinges on a healthy spawn. The tiny eggs are key.

In this May 8, 2014 photo, a wildlife biologist holds a handful of sand containing dark green horseshoe crab eggs on a beach in Middle Township, N.J., along the Delaware Bay. (AP Photo/Wayne Parry)

“I like to explain the trek as a ladder. Each stop is a rung, and one broken
rung jeopardizes the entire journey," says Deborah Cramer, author of *The Narrow Edge: A Tiny Bird, an Ancient Crab, and an Epic Journey*. In researching for its publication, Cramer followed the red knot from the southernmost tip of the South American mainland to the Arctic tundra.

The Delaware Bay is home to the largest spawning horseshoe crab population in the world, and in turn, “the Delaware Bay Estuary is the largest staging area for shorebirds in the Atlantic Flyway,” feeding an estimated 425,000 to 1 million migratory shorebirds each year, according to the Atlantic States Marine Fisheries Commission (ASMFC).

Since the early 1990s, there has been a huge decline in shorebirds on the Delaware Bay. According to a recent New York Times article, red knot numbers have dropped as low as 10,000 in some years since 2000, which is about one-ninth of the population witnessed in the 1980s. The bird may, according to some, be at imminent risk of extinction.

The idea of a ladder-like trip, with each stopover as a rung, is a point Cramer reiterates in her book. “Some are already broken. Some are being repaired. Others are in danger of breaking. The story and struggle of *rufa* red knots is the story and struggle of all knots, and millions of shorebirds,” she writes.
When the red knot started to decline it was clear the species had a competitor. That competitor was, of course, humans.

**Blue blood and a life-saving protein**

We tend to think of the food chain as a single-file, one-way succession of creatures, with humans and beasts on top, but reality and nature are much more complicated than that. The system is more of a web, with many creatures relying respectively on each other in symbiotic and otherwise intricate relationships. It gets even more complicated when you consider less traditional means of consumption, such as our reliance on the horseshoe crab.

In Asia, they’re a food source. But across the globe, horseshoe crab blood, rich in copper and brilliantly blue in color, is used to detect endotoxins in food and drugs.
In the 1960s, some of Jack Levin’s colleagues were questioning his studies of horseshoe crabs with medical researcher and Johns Hopkins professor Frederik Bang. They wondered what a hematologist was doing in the Marine Biological Laboratory in Woods Hole, Massachusetts.

In the early days of injectable drugs, it was common to develop a fever after being injected. So common, in fact, that the then-phenomenon was known as “injection fever,” according to the U.S. Food & Drug Administration. Fever, and even death, can occur when endotoxins are introduced into the blood during an injection. From the 1940s to the 1970s, injections were tested for illness-causing endotoxins by injecting rabbits with the drug or product to determine whether it had been contaminated. Not only was this considered inhumane by some, it was expensive and time consuming.

“I realized that the horseshoe crabs’ clotting was much more sensitive than rabbits, and scores more sensitive than had ever been described or discovered,” Levin says of his studies at the Marine Biological Laboratory.

From this discovery, the *Limulus* amebocyte lysate (LAL) test was born, named for the *Limulus polyphemus* horseshoe crab species, found along the Atlantic coast of the U.S.

Amoebocytes in the horseshoe crabs’ blood contain an especially sensitive clotting factor that is activated in the presence of endotoxins—a component of the exterior cell wall of illness-causing bacteria, like *E. coli*. The LAL test is now used to test vaccines, medicines, food and water all over the world, and the resulting indicator is one of the most valuable liquids on the planet, worth $35,000 to $60,000 per gallon, according to The Guardian.
Horseshoe crabs in a rack bleed into bottles at the BioWhittaker lab in Chincoteague Island, Va. in an August 2000 photo. The blue blood is the only source of a compound used to test for contaminants in every drug and vaccine, every artificial limb, and every dialysis and intravenous drip. The crabs are returned to the sea the next day. (AP Photo/Steve Helber)

Levin is proud, and he should be. His discovery has kept countless people, and even pets and other domesticated animals, healthy. His achievements with Frederik Bang in endotoxin detection landed the horseshoe crab on the Johns Hopkins list of 100 Objects That Shaped Public Health along with the ambulance, the electron microscope and the birth control pill. Levin makes it clear that he has the scientific method and scientific community to thank for his success.

“Here’s an example of basic research leading to a gold standard in the medical industry,” Levin lectures. “In this political climate, there unfortunately isn’t always a ton of respect for the scientific method and community.”
The U.S. Food and Drug Administration approved LAL testing in 1977, and from there the technology took off in the pharmaceutical arena, becoming the most widely used endotoxin test in the world.

And a new stressor began to affect the horseshoe crab population.

**Classic consumption**

Yum Kai Meng Da is a delicacy in Thailand. Though the horseshoe crabs provide little meat, the roe, or eggs, are mixed into a spicy salad or eaten right out of the arthropod itself, often served as street food. The roe is served similarly in Malaysia.

Overfishing of horseshoe crabs for human consumption, as well as for Tachypleus amebocyte lysate (TAL), the similarly sensitive clotting factor found in Asian horseshoe crabs, is a big problem in Asia. There are three Asian horseshoe crab species, all of which are believed to be endangered.

“The truth of the matter is we’re only one step removed from human consumption, because we use these animals for bait, but we use the bait to catch whelk and eel, which we eat. So in a sense, we have a human consumption market for horseshoe crabs too,” Glenn Gauvry, founder and president of Ecological Research and Development Group (ERDG), which has a mission to conserve the world’s four horseshoe crab species, said of the U.S. fishing industry.

According to the ASMFC, between the 1850s and the 1920s, 1.5 million to 2 million horseshoe crabs were harvested each year in the U.S. for use as fertilizer and livestock feed. Harvest decreased in the 1950s and was nearly zero in the 1960s, and varied widely between the 1970s and 1990s. Commercial harvest then shifted largely to bait for whelk and eel fisheries, leading to a record of nearly 6 million pounds in 1997.

“The ASMFC regulates a lot of fish harvest along the East Coast, including
things that are not actually fish, like lobsters,” said Jean Woods, curator of birds at the Delaware Museum of Natural History. “It’s not actually a federal agency, so it’s not a mandated thing. It’s more consensus-based. Each of the states has a seat at the table, and they come to consensus on how to manage all of these different types of fisheries.”

Though, according to the Commission’s 2019 Benchmark Stock Assessment, the ASMFC does not have all the information needed to determine whether horseshoe crabs meet the definition of an overfished population in the U.S., regulations were placed on commercial harvest of horseshoe crabs throughout the late 1990s and early 2000s in the Delaware Bay and along the Atlantic Coast in response to declining numbers and growing demands. However, given the 2019 assessment results of low fishing mortality and relatively high abundance, overfishing and an overfished status are currently unlikely for female horseshoe crabs in the Delaware Bay region. Woods, who works closely with the Delaware Shorebird Project to mitigate threats to the red knot and other shorebirds, said that regulations forbid harvests during the period when shorebirds descend on the Delaware Bay beaches. It’s also now illegal to harvest female horseshoe crabs from the Delaware Bay for bait, as saving one female could result in the survival of future generations.
Male horseshoe crabs approach a large female horseshoe crab during spawning season along the Delaware Bay. Several males may fertilize a single female’s eggs, making for a variety in genetics and greater chances of species survival. Barnacles can be seen growing on their shells. (Alex Wroblewski)

New Jersey has prohibited commercial harvest of horseshoe crabs since 2008. However, it is still completely legal for fishermen in New Jersey to purchase the bait caught in other states’ waters, and dealers travel from up and down the Atlantic Coast to fill demands in the Garden State, the Press of Atlantic City wrote in June.

In Asia, harvests are largely unregulated, and a black market sometimes dodges what scant regulations do exist. As all indications point to a diminishing resource in Asia, there’s a possibility this may drive up the demand for the American LAL.

“With the United States horseshoe crab population just beginning to show signs of recovery after years of decline, it is questionable whether the U.S. horseshoe crab population can manage the growth of the LAL consumer
market, much less the TAL consumer market, if there were to be an issue of supply and demand,” Gauvry has written. “Is it wise to have the global healthcare industry so directly tied to a diminishing and/or marginally stable resource?”

**Environmental pressures**

Though they’ve survived the earth’s most volatile states in prehistory, horseshoe crabs are not completely armored against our fast-changing climate and current environmental stresses. Overharvesting for bait, human consumption and for LAL and TAL all compound the damage coastal development and climate change’s rising seas have on all four species.

“The biggest threat globally, and this would affect all four species individually, is loss of habitat,” explained Gauvry, “followed by human consumption, followed by use in the biomedical industry, but the biggest is loss in habitat.”

Gauvry says this is mostly human-driven. Coastal development eats into horseshoe crab spawning areas, and it’s a pattern that can be seen affecting the American horseshoe crab population, as well as the three subspecies in Asia.

It’s predicted that horseshoe crab populations off the East Coast of the U.S. will decrease by 30% in the coming decades, and the decrease of the Asian subspecies is expected to be even more dramatic.

“Through Malaysia and Indonesia, Thailand, where there’s a lot of mangroves, one of the species is a mangrove species,” Gauvry says. “We’ve lost half of our mangroves in those areas of the world with land being reclaimed for palm oil plantations, rice plantations. There’s also a lot of infrastructure and economic development type of land reclamation projects, so the mangroves aren’t there anymore.”
Gauvry says Americans are just as guilty. “We tend to have more fancy homes along our coastlines, not palm oil plantations, but the result is the same. We’re basically fragmenting and claiming these habitats for purposes other than horseshoe crab spawning.”

Beach erosion compounds this issue, as each centimeter of sea-level rise will be accompanied by a loss of about a meter of beach, according to Physics Today. Delaware’s beaches, including the Delaware Bay, saw significant erosion in 2018 during Winter Storm Toby. During Hurricane Sandy, New Jersey beaches along the Delaware Bay, some of which also host a large horseshoe crab spawn, lost 2 to 3 feet of beach, according to the U.S. Department of the Interior.

A horseshoe crab makes its way back to the water during the 2019 spawning season along the Delaware Bay. (Alex Wroblewski)

In addition to beach erosion, warming waters could move the horseshoe crab spawn weeks earlier. There is a possibility that this could throw off the
red knot journey, leaving them without enough food to complete their migration north. Scientists are unsure of how a warming planet could affect the red knot’s migration. Will the birds leave Tierra del Fuego earlier, or maybe later? Will they miss the spawn? Will they change course and change feast? Or will they die out?

Unlikely allies in conservation

Dense armor makes horseshoe crabs nearly impervious against predators in the water, but their strong tail or a helping human hand is the only hope when a rough tide kicks a horseshoe crab onto its back on the beach.

And that’s why a group of about two dozen conservationists, birders and pharmaceutical and biotechnology representatives gathered at Pickering Beach on the Delaware Bay on June 4 to flip horseshoe crabs right-side-up. It’s not a group that anyone would think to lump together. But when it comes to horseshoe crabs, they’ve got a common goal: Save them.

The horseshoe crab has been Delaware’s state animal since 2002, which was still the early days of conservation efforts for the animal.

Gauvry, who’s also mayor of the Delaware Bay area town of Little Creek, wears a pewter horseshoe crab pin on the collar of his athletic shirt, and says he tries to remember to give one to anyone who comments on it. “One of the things that is always a little bit disheartening is that if it were not for a rather large and avid birding community that takes great interest and pride in the understanding and protection of bird species, there probably wouldn’t be quite as much attention to horseshoe crabs as there is today.”
A horseshoe crab lays on its back, with its ten legs and tale visible. (Alex Wroblewski)

Allen Burgenson is the Global Subject Matter Expert for Endotoxin Detection
at Lonza, one of the world’s leading biotechnology companies. He also serves as chair of the Horseshoe Crab Advisory Panel of ASMFC.

This isn’t a story about the big, bad pharmaceutical industry. Many a story delves into the industry’s flaws, but the use of LAL tests keeps humans safe every hour of every day.

“The global pharmaceutical industry never handles a single horseshoe crab. They just buy the test,” Gauvry explained. “They buy the test from only a handful of companies.”

One of those companies is Lonza. It’s clear that the pharmaceutical industry is only going to grow, and it’s clear to individuals within the biotechnology industry, to birders, to conservationists, that LAL uses a finite resource.

This spring, Burgenson, along with another Lonza employee, footed the bill to help fund a 350-foot temporary fence along a section of Pickering Beach where horseshoe crabs kept dying.

According to Gauvry, sand-shifting nor’easters over several years helped to create a sandy protrusion in one section of beach. The beach rises and then falls into a pond and stream, where spawners were getting stuck.

The new fence allows the tide to rise like normal, but the crabs are stopped from getting washed too far up the beach. According to ERDG, the fence could save thousands of horseshoe crabs each spawning season. The fence is removed each July after spawning season ends.

“If we do something bad for the horseshoe crab, we’re not gonna have the horseshoe crab as a resource anymore,” Burgenson said. “So we believe it is our responsibility to take care of it and make sure that there’s an abundance, not only for us, but for the shorebirds.”

Since the late 1990s, the ASMFC’s regulations and horseshoe crab population management plans throughout its entire range, from Maine to
Florida, have helped to maintain a marginal stability in the animal’s numbers.

“It created a fisheries management plan solely for the purpose of maintaining a sustainable horseshoe crab population that could be enjoyed by the birds, enjoyed by people, harvested for bait by the conch and eel industries and harvested by the biomedical industry for endotoxin testing,” said Gauvry. “That plan has been successful.”

In the U.S., the biomedical industry is permitted to harvest a regulated number of horseshoe crabs. The crabs are bled for about 30% of their blood and released. There are, of course, casualties. ASMFC reports a 15% mortality rate, and most other current estimates cite a 5% to 20% mortality rate. On Delaware’s shores along the Delaware Bay, 500,000 male crabs are permitted for bait harvest each year. The ASMFC’s most recent data collection clocks 2017’s bait harvest along the Atlantic Coast at about one million, and biomedical harvest at just under 500,000 horseshoe crabs for the same year—the largest harvest since 2003, but still well under the coastwide quota.

In Asia, where regulation is lacking, the crabs are bled to death for TAL and then sold for human consumption—a 100% mortality rate. When it comes to fishing for bait in the U.S., that is indeed a 100% mortality rate as well.

It’s a slow game. Horseshoe crabs mature slowly, growing as they molt. It takes 9 to 11 years to reach age of reproduction; females take one year longer than males, molting one additional time. Any rebound in population takes about a decade to become apparent in the spawn.

“What we do today that might start having a positive effect on the species might not be seen for 10 to 12 years,” Gauvry explained. “We’re starting to see the benefits of management today from what was done years ago. Each year we should see incremental changes, but you’ll never see dramatic changes.”
Throughout most of its range, the American horseshoe crab population has been recovering as a result of the ASMFC regulations. It’s now reported as stable throughout most of its range, but still suffering in the New York area. Gauvry said that a shorebird increase has been witnessed as well.

“Our story is pretty good, coming from a not-so-good past around 1978,” he said. “In Asia, though, it’s another story. There’s no regulations, hardly at all, on these populations, so between unregulated harvest and loss of habitat, all three Asian horseshoe crab populations are threatened or endangered and at risk of local extinction throughout their entire range.”

A better solution may be on its way, but it’s not without complications.

Jay Bolden is a senior consultant biologist at Eli Lilly, which sells pharmaceutical products in about 120 countries. Bolden is also a birder, who doesn’t believe his two passions need to be at odds.

The late-morning tide rises, washing thousands of horseshoe crabs onto Pickering Beach, and Bolden explains his hope for the future of his company as he helps the creatures back onto their feet. He’s an attendant at the fifth annual Global Endotoxin Testing Summit hosted by Lonza, and one of dozens of horseshoe crab helpers on June 4, which also include Gauvry, Burgenson, Levin and Cramer.

Bolden was no stranger to the complicated web involving the threatened shorebirds, the biomedical industry and horseshoe crabs, but it was this very summit five years ago that inspired Bolden to make some changes in his industry, especially, Audubon reported, after learning that Eli Lilly planned to open a plant in China that would require endotoxin testing.

Bolden has been a driving force in convincing Eli Lilly that a synthetic enzyme called recombinant factor C (rFC), is the ethical alternative to LAL. Making the switch could mean no more biomedical horseshoe crab harvests, and according to Bolden, rFC is more efficient and cost-effective.
While rFC has been on the market for over 15 years, changing a biomedical standard is difficult to say the least. Just like the switch from rabbit testing to LAL took over a decade after Levin and Bang’s discovery, an entire upheaval of processes takes time. Burgenson tried for years to get the FDA to approve rFC. They denied approval until 2012. He petitioned the U.S. Pharmacopeia, the country’s official book of approved drugs and medication. They have yet to list the alternative. And if a substance isn’t listed in the Pharmacopeia, even if approved by the FDA, it isn’t widely trusted.

The European Pharmacopeia listed rFC usage in 2016. The slow progression is a matter of trust, a matter of money, a matter of interest, and a matter of safety.

After years of studies, Bolden got his okay. In November 2018, the FDA approved the usage of rFC to test a migraine prevention drug. It was the first drug to be released after using the alternative to LAL. By 2020, Eli Lilly expects to be approximately 90% converted to rFC usage at its internal sites.

Bolden, along with other concerned biologists, birders, fishermen and conservationists, hopes other companies will act fast to keep up, and to keep the important resource, horseshoe crabs, stable.

450-million-years strong

Horseshoe crabs are a generalist species, making them able to evolve to adapt to a wide variety of environmental conditions, including those created by humans. It’s one of the main reasons they’ve survived on this planet for so long.

“We know that there’s genetic differences within the population along its spawning range, and that’s important because it’s not one homogenous population from Maine to the Yucatan,” Gauvry said. “If you wipe out all of
the crabs in Maine, or you wipe out all the crabs in the Yucatan, you’ve wiped out some of the genetic variation that has helped this animal survive for 450 million years because they’re generalists.”

In essence, Gauvry said, what worked in Maine might keep the arthropods alive a million years from now. What’s working for the animals now in the Delaware Bay may completely fail as our climate changes, as human development changes the coastlines, or as any number of unexpected and unpredicted events across the globe change the horseshoe crabs’ population. Right now, somewhere on earth, a genetic grouping of the crab is most likely developing what the animals need to survive the upcoming era of change.

“One of the things to keep in mind with this species is that they’ve been around for so incredibly long. They were around when we didn’t have the continents that we have right now — when the oceans that we have names for weren’t the oceans at that time,” Gauvry said.

The ASMFC and ERDG work to regulate the horseshoe population, and also to ensure that the needs of both the fishing and biomedical industries are fulfilled, but some critics have said that the regulatory bodies are too close to the pharmaceutical and biomedical industry, The Guardian reported. Gauvry insists that cooperation is how changes are made.

“We work with all of them, with the exception of TAL companies, because we’re all trying to get them to use best practices in terms of how they handle horseshoe crabs, and we’re also trying to work to get the industry, the pharmaceutical and biomedical industry, aware that there are alternatives, and maybe they should start using them,” Gauvry said. “I’ve been doing this for a long time with the pharmaceutical industry and we’re making progress because we’re working with them, and we understand the complexity of understanding the shifts like this from one technology to another.”
Balancing the demands of two separate industries and preserving the resource for future generations is a delicate and precarious dance. In a perfect world, the shorebirds would also get their fill.

Cramer has the red knot in mind when she says conservation could be more aggressive. She worries of the many things taken from the birds, from moments feeding on the beach disturbed by a walker’s excited dog, to inches of beach from climate-change-driven sea rise, to their dwindling food source.

“You don’t realize when you’re walking along the beach and see a flight of sandpipers, a beautiful sight, that you’re disturbing them,” Cramer says. “You’re taking time from them.”

“All we need to do is create an opportunity for the horseshoe crabs, and they will survive,” she says as high tide ends along Pickering Beach.

Of the red knot, we can’t be certain.
Horseshoe crabs populate Pickering Beach along the Delaware Bay during the 2019 spawning season. The Delaware Bay is home to the largest spawning horseshoe crab population in the world. (Alex Wroblewski)

*Published July 24, 2019*