Using mathematics to understand disease eradication: Guinea Worm Disease points the way forward

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In recognition of the Mathematics of Planet Earth 2013, a French version of this article has also been featured in Accromath (http://accromath.uqam.ca).

How can we actually eradicate a disease? And why aren't we better at it? We have a very poor record of disease eradication. In the entirety of human history, we've successfully eradicated just two diseases: smallpox and rinderpest (the latter a cow disease, declared eradicated in 2011). Our "model" for what it means to eradicate a disease is thus based on what worked for these two diseases: a successful vaccine.

Guinea Worm Disease tells a different story and one that may illuminate a new way forward. Guinea Worm Disease is a parasitic disease, spread via drinking water, that has been with us since antiquity (it's mentioned in the Bible and Egyptian mummies suffered from it). Essentially, the parasite attaches itself to a water flea, you drink the flea and your stomach acid dissolves the flea, leaving the parasite free to invade your body. Because of gravity, it usually makes its way to the foot, where it lives for an entire year. **See Figure 1.**

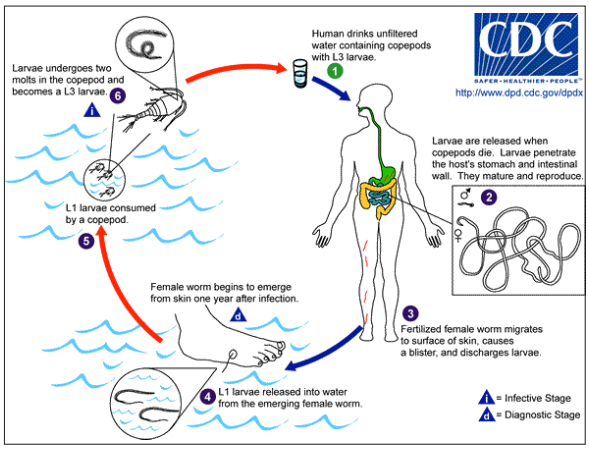


Figure 1: The life cycle of Guinea Worm disease. *Image copyright the United States Centers for Disease Control and Prevention.*

After a year, your foot is burning and itching, so you put it in the water. If your village only has one water source, then that often ends up being the drinking water. At this point, the fully grown worm bursts out of your foot, spraying forth 100,000 parasites and restarting the process. **See Figure 2.**



Figure 2: A Guinea Worm.

In the 1950s, Guinea Worm Disease affected 50 million people across most of Africa, Asia and the Middle East. Today it's on the verge of being eradicated, with less than 2000 cases, in just four African countries. Ghana was declared worm-free in 2011 and the disease primarily persists in South Sudan, as a result of the Sudanese civil war. This ancient scourge is almost gone. **See Figure 3**.

So what happened? Before we reveal the answer, let's think about how you might eradicate a water-borne disease (i.e., a disease transmitted through contaminated water).

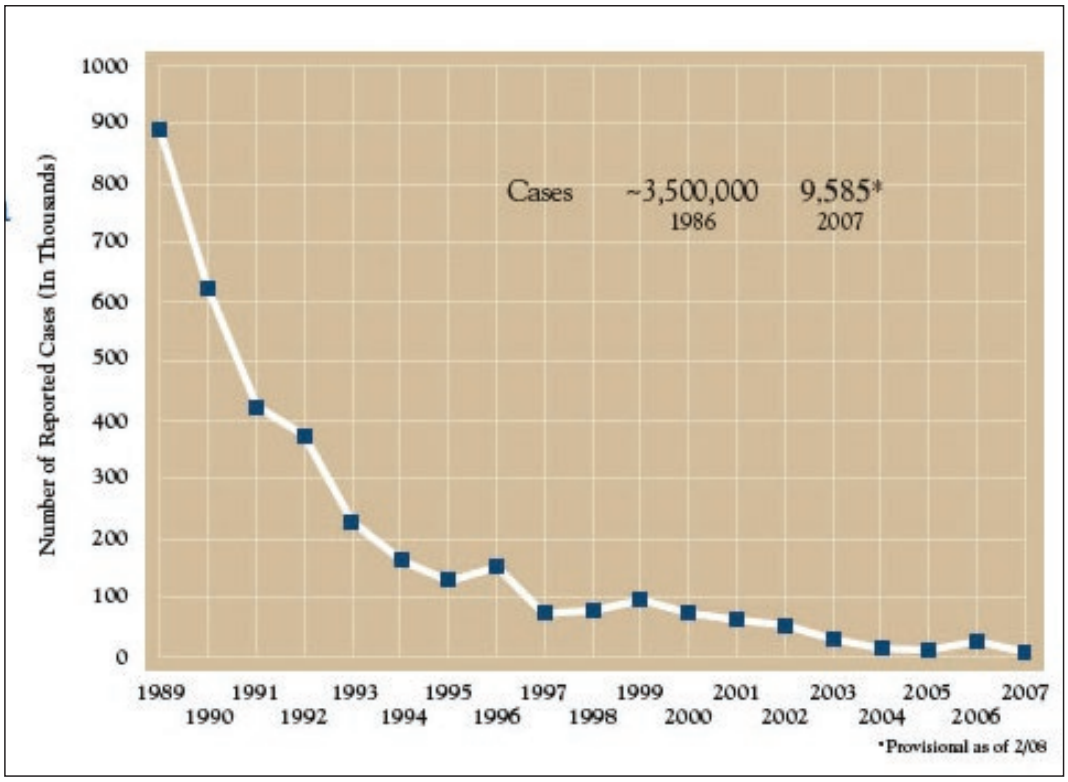


Figure 3: The decline in Guinea Worm Disease cases over the past 25 years.

Possibilities are a vaccine, drugs that treat symptoms, chemicals that kill the parasite, better hygiene or education that changes people's behaviour. Unfortunately, there is neither a drug nor a vaccine to treat Guinea Worm Disease. So let's see what mathematics tells us.

Mathematical modelling of infectious diseases is a fairly new topic that has had significant success. It has been useful in programs dealing with malaria control, smallpox eradication, mosquito management, climate change and emergency preparedness. Where modelling works well is in quantifying measurable things, like drugs, vaccines or insecticide. Where it has more trouble is with messy and unpredictable variables, like human beings.

Incorporating human behaviour into models is complex and requires an understanding of the ethical, sociological and biomedical factors inherent in tackling a disease. This requires interdisciplinary research across the traditional boundaries of social, natural and medical sciences.
To create a mathematical model, we need to keep track of what comes in and what goes out. In the case of Guinea Worm, we divide the population of humans into three subcategories. The first category is susceptible individuals; three things can happen to them: they are born, become infected or die. The second is infected individuals, who either become infectious or die. The third, infectious individuals, either recover or die. We also have a population of worms: the parasite is born when infectious individuals put their foot in the drinking water (because fresh water produces relief) and dies shortly thereafter. Guinea Worm disease is not lethal, so each time we speak of death rate, it is the usual death rate.

Combining these, we develop a system of differential equations that describes the rates of change of every variable. This system is kind of an "engine of change." With a starting key (the initial conditions), we can then use our engine to predict the future. This procedure works if we've gotten the mechanics of the interactions right.

Modelling is like map-making.

You don't want a map to be a perfect representation of reality, because that would be too cumbersome. Instead, you want the salient features, scaled down to a usable size.

So modelling isn't trying to mimic reality, but instead it's providing a useful roadmap so you can navigate the future. **See Figure 4.**

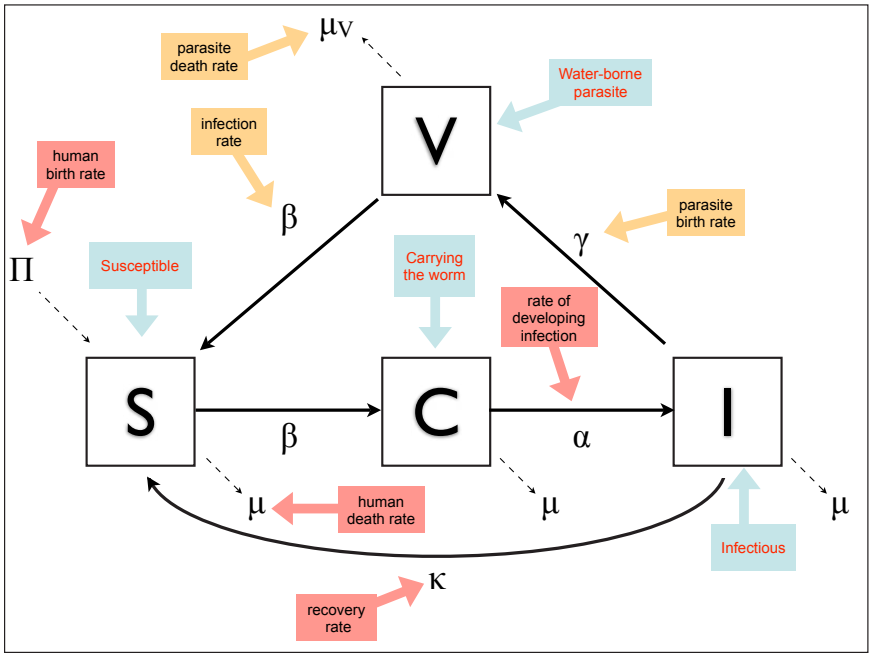
How do we know when we've eradicated a disease? Or at least when we're moving in the right direction?

This issue vexed public health officials in the early twentieth century when they were trying to eliminate malaria from places like the United States and Canada. Sir Ronald Ross won a Nobel Prize for demonstrating that malaria was spread by mosquitos (rather than toxic vapours, as was previously thought). However, this led to some despair, because it was realised that you couldn't eliminate all the mosquitos. Nor would you want to, because they prop up our ecosystems.

Ross's breakthrough came when he realised that you didn't have to kill every mosquito, but rather just a critical number of them.

This is essentially the "tipping point" of a disease: if each infected individual causes more than one infection, then the disease will spread.

Figure 4: The mathematical model. Humans can be born, become infected or die (from background reasons, not from the disease). Once infected, humans carry the worm for a year, before becoming infectious (for a few hours). The parasite's birth is proportional to the number of infected individuals, while its death rate is proportional to the size of the population.



However, if each infected individual results in less than one infected individual, then the disease will eventually die out.

This concept is called R_0, the basic reproductive ratio (pronounced "R nought"). R_0 measures the average number of secondary infections that a single infectious individual will cause. So if each infected individual infects three people, they infect three each and so forth, meaning the disease spreads like wildfire. On the other hand, if $R_0 < 1$ (so that ten infected people infect nine, those nine infect eight and so on), then the disease will die out on its own.

If we can estimate R_0 from our mathematical model and then determine which parameters will reduce it below one, then our job is done. With those control measures in place, the disease will eventually be eradicated. R_0 helps us understand which control measures will be helpful and how intensely they should be applied.

In our case, the basic reproductive ratio is

$$R_0 = \frac{\Pi\alpha\gamma\beta}{\mu(\alpha+\mu)(\varkappa+\mu)\mu_V}$$

We have three factors under our control: increasing education (which will reduce the parasite birth rate γ), reducing transmission (which will reduce β) and chlorination (which will increase the parasite death rate μ_V). You can see how R_0 depends on all these factors. So applying any one of them should reduce R_0.

That isn't the end of the story, however. Although we have identified the beneficial factors under our control, we don't necessarily achieve eradication. And every parameter will vary, in practice, because some worms will give birth to more parasites than others or some people will be more likely to be infected.

So we need to account for variations in our parameters. Fortunately, determining parameter ranges is much easier than pinpointing a precise value. The three parameters under our control are γ, β and μ_V, so let's vary these over large ranges while fixing all other parameters at their average values. **See Figure 5.**

Killing the parasite isn't terribly effective. Why? Increasing the parasite death rate involves moving along the μ_V axis to the rear left. But the level surface is very shallow, so you need to move a long way to the back corner to get under the surface. Reducing transmissibility involves moving down the β axis. But this is on a log scale, so that takes much longer than it first appears. However, see how steep the surface is for small γ? This makes it very easy to move under it by a small change in γ. This suggests that eradication should occur if we stick to one strategy: reducing the parasite birth rate.

How can we do that?

Through education, of course!
Encouraging people not to put their infected limbs in the drinking water means that each time a worm doesn't burst into the water, that's 100,000 parasites that aren't released.
This means that, in the final push to eradication, we should concentrate our efforts on reaching remote communities, informing them about the specifics of Guinea Worm Disease and its transmission cycle.

In summary, eradicating a disease isn't just a matter of sitting around and waiting for someone to invent a vaccine. We have vaccines for less than 2% of all diseases. Both drugs and vaccines are beholden to scientific breakthroughs that consume millions of dollars but may never happen. However, education is relatively cheap, highly effective when done right and can begin immediately.

The critical element of this is getting education right. Done badly, it can look to developing countries as though the West is telling them what to do (e.g., people often reject messages about safer sex due to histories of population control).

However, culturally specific education, carefully targeted towards its audience, has the potential to change entire societies, as it has with Guinea Worm Disease.

Mathematical modelling can help us determine what needs to be done in advance and to determine which factors will have the greatest impact on the outcome. We are close to eradicating Guinea Worm Disease, one of humanity's oldest diseases, thanks to behaviour changes and education alone. Once Guinea Worm Disease is eradicated, its lessons will apply to other diseases where education can be effective, not least of which is HIV. Messages need to be carefully positioned and targeted, but if done right they have the potential to do what no amount of treatment has managed: turn a global epidemic around, using the power of education.

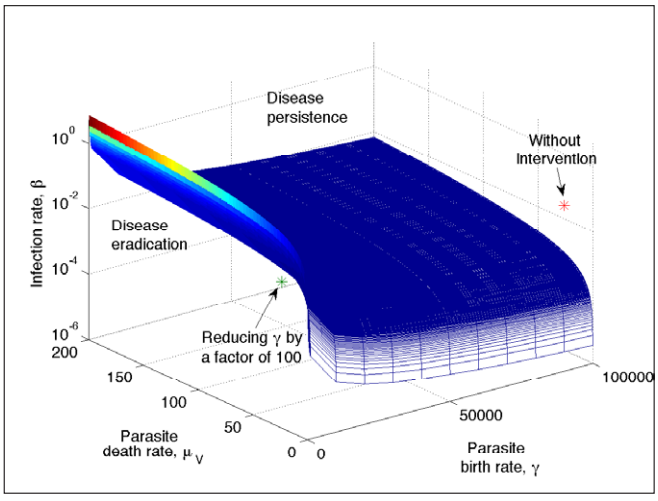


Figure 5: The level surface $R_0(\gamma, \beta, \mu_V) = 1$. If you are above the surface, then R_0 is greater than 1 and the disease will persist. If you are below, then R_0 is less than 1 and the disease will be eradicated.