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The Global Problem of Antibiotic Pollution

Large amounts of antibiotics are used in human medicine and in agriculture. For example, in the UK, we use around 650 tonnes of active ingredients. Following administration, these molecules will be absorbed to varying extents and may then be metabolised to some degree before being excreted in the urine and faeces. The antibiotics are then transported to the natural environment, *via* the wastewater network, application of manures and sludge to land as a fertiliser and from excretion to pasture systems (Boxall, 2004). Manufacturing, disposal of unused medicines and aquaculture are other sources of emissions to the environment. When metabolism and removal of antibiotics is factored in, we estimate that approximately 250 tonnes of the 650 tonnes are emitted *via* these pathways to the natural environment in the UK.

In the late 1990s, the scientific community began to recognise that the excretion of antibiotics and other pharmaceuticals to the natural environment could result in contamination of rivers and soils and, due to the fact that these molecules are designed to be biologically active, they could be negatively affecting ecosystem health (Daughton and Ternes, 1990). In the late 1990s the first extensive monitoring campaign for these molecules was done on the River Rhine in Germany (Hirsch *et al*., 1999) and in the early 2000's a major US study was performed to monitor pharmaceuticals in waters taken from 139 sites across the country (Kolpin *et al*., 2002). Not surprisingly, in these studies antibiotics and other pharmaceuticals were detected at many of the sites studied at concentrations in the 10s-100s of ng/L. Since then, similar studies have been done in other countries and exploring other environmental media such as soils, sediments and ground waters. By 2016, more than 1000 publications had been published in the scientific literature reporting the occurrence of pharmaceuticals in the environment. Taken together, these studies show that the contamination is a global issue (Aus der Beek *et al*., 2016).

Many scientists believe that the observed occurrence of antibiotics and other pollutants, such as metals, in environmental media is contributing to the global antimicrobial resistance (AMR) crisis. Although flawed, the O'Neill Report recently predicted hundreds of thousands of people would have died from resistant infections in 2016 and millions might die annually by 2050 unless action is taken to curb AMR evolution and dispersal (DoH, 2016). While antimicrobial resistance is a natural phenomenon, many are concerned that chemical pollution by antibiotics has contributed to elevated levels of resistance by selecting for resistance or by promoting horizontal gene transfer of resistance genes within bacterial communities in the environment (Wellington *et al*. 2012).

Antibiotic manufacturing, in particular, is believed to be an important contributor to pollution-induced elevated resistance levels in the environment. In 2007, a study in the Hyderabad region of India detected ciprofloxacin, a fluoroquinolone antibiotic, at levels up to 30 mg/L in a tributary of the Ganges River that was receiving untreated manufacturing waste (Larsson *et al*., 2007). To put this into some context, this concentration is higher than levels that would be seen in the bloodstream of a patient being treated with the antibiotic. Recognising the importance of this issues, the AMR Industry Alliance, an alliance of over 100 biotech, diagnostics, generics and research-based pharmaceutical companies and associations, have recently proposed 'safe' limits for antibiotics in discharges from manufacturing site (Tell *et al*., 2019). The idea is that, if these limits are implemented at manufacturing sites across the globe, concentrations in the environment will drop to levels below those that result in elevated resistance.

There is some debate about the accuracy of these 'safe' limits but they do now provide a basis to assess the potential contribution of the concentrations of antibiotics that are being detected in water bodies around the globe to the AMR problem. By comparing reported concentrations at a site with the limits, it will be possible to see whether the limit is exceeded or not and hence identify hotspots of risk of selection. This could help to establish the polluting activities that are contributing most to the problem but also identify areas where mitigation activities can be focused.

While such an assessment would be incredibly valuable, the existing monitoring data do not have the coverage to fully understand the scale of the issue around the globe. Aus der Beek *et al*. (2016) established that data are available for 71 countries worldwide. For some of these countries, data are only available for a handful of antibiotics. Most data are from studies in western Europe and the US with data for China and India becoming increasingly available. For the entire African continent, only 23 publications were identified with regional representation mainly from South Africa, Nigeria, and Kenya. Due to differences in antibiotic use, regulation, levels of connectivity to waste and wastewater treatment and management systems and performance of treatment technologies, we expect that many of the countries where few or no monitoring data are available will have higher levels of antibiotic pollution than the well-studied regions.

To address the large gaps in our knowledge of antibiotic exposure in river waters across the Globe, over the past two years the University of York have been working with a consortium of 88 scientists from across the globe on a unique monitoring exercise 'The Global Monitoring of Pharmaceuticals

Project' (see www.globalpharms.org). Samples have been taken from multiple points (usually between 6 and 10) on rivers across 101 countries and analysed for 61 pharmaceuticals including 13 antibiotics. In some countries, multiple rivers have been monitored. The study will finish at the end of the year but we already have data on concentrations at 768 sites taken across 72 countries and covering 91 river systems.

Based on the results analysed so far, antibiotics are detected at 65% of the sites sampled. No antibiotics were detected in 17 of the 91 river systems and three antibiotics (amoxicillin, cloxacillin and oxytetracyline) were not detected in any sample. Amoxicillin is one of the most used antibiotics but we think the lack of detection is due to the fact that it degrades quickly in water. Generally, levels in low and middle income countries are greater than in high income countries. Highest total antibiotic concentrations are seen in rivers in Bangladesh, Kenya, Ghana, Nigeria, Pakistan, South Africa, Israel, Tanzania and Spain with the highest total concentration seen in the Kirtankhola River in Bangladesh at a level of approximately 40 µg/L. The most frequently detected antibiotics were trimethoprim, sulfamethoxazole and ciprofloxacin which were seen in over a quarter of the water samples.

Comparison of the measured levels of individual antibiotics with the AMR Industry Alliance 'safe' levels shows that in 38 river systems, antibiotic levels are below the 'safe' limit. At two river systems, one in Cyprus and one in Iowa in the US, concentrations of at least one antibiotic were above 'safe' levels at all of the sites sampled. The highest levels of exceedance were seen in Bangladesh, Ghana, Kenya, Nigeria and Pakistan with metronidazole, sulfamethoxazole and clarithromycin exceeding the 'safe' levels by the highest degree. The highest risk site was in Bangladesh where metronidazole exceeded the 'safe' limit by 300 x.

When performing the sampling, the monitoring teams noted background information on each site and also took photographs of the sampling point and surrounding area. Examination of this meta data indicates that highest levels of antibiotics are seen at sites: close to poorly managed waste dumps; receiving inputs from pharmaceutical manufacturing; with extensive littering with waste along the river bank; receiving piped inputs of untreated sewage; and where exhauster trucks (which collect human waste from pit latrines) discharge their waste.

Overall our study shows that rivers around the World are awash with antibiotics. A significant proportion of the worlds rivers have concentrations of antibiotics of concern. Highest levels of exceedance of 'safe' limits for antibiotics are seen in low and middle income countries although there are situations in high income countries where the limits are also exceeded.

Our findings suggest that antibiotic pollution could be playing a role in the AMR crisis. Alongside other initiatives to solve the AMR problem such as controlling the over-use of these molecules, we should urgently be working to lower the levels of antibiotics being emitted to the natural environment. Better waste and wastewater management around the world will not only bring down levels of antibiotics in rivers and soils but will also deliver wider benefits to human and ecosystem health.

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Arden Andersen DO, MSPH, PhD

Bard College Microbiome Conference Position Paper

Thank you for the invite and the distinguished group of speakers, sponsors and participants.

Much discussion, research and extrapolation have been associated with the microbiome - the microorganism community ubiquitous to every living thing on planet earth. Historically, microorganism research has been focused primarily on one perspective - pathology - meaning the association with disease and microorganisms.

During the period between 1665-1683 Robert Hooke and Antoni van Leeuwenhoek, fabricating and using simple microscopes of 25 to 150 power, discovered and described protozoa and bacteria. Little was done for about 150 or so years with that information regarding medicine and public health.

Ignus Semmelweis MD in the early 1800's, first suggested something "unknown" (which caused child birth fever and maternal death) was being transferred from the morgue to the delivery room via the dirty hands of doctors. John Snow MD then discovered that the cholera epidemic in London in 1846-1860 was water borne. Subsequently, Louis Pasteur is credited with pasteurization to kill microbes as well as vaccinations to immunize people against infections.

Over the next 150 plus years the primary focus, regarding microbial research, has been and still is for agents to isolate, identify and kill specific pathogenic organisms. It has spawned a multi-billion dollar industry, funds thousands and thousands of institutional and private research departments and has imprinted upon the general public the very limited "belief" that "bugs" are bad. It has fostered a near paranoia regarding environmental exposures to nearly any and everything. A culture of "fear" has been perpetrated to continue the profitable half-truth.

New and continuing research over the past few decades, particularly with the advent of PCR and genomic testing, has revealed that the number of microorganisms that are truly pathogenic compared to the total number of microorganisms on the planet or simply in our own body is a very small number. In fact, most pathogens are only situationally pathogenic, meaning only a problem when the overall microbiome becomes disrupted or out of balance in some way.

This is true from the soil to the insect to the animal to the human organism and their microbiomes. Without the microbiome the oceans are dead. Without the microbiome humans are dead. Without the microbiome the soils are infertile and unproductive. These realizations have led to the belief and contention that the microbiome is the key to healing the planet from centuries of pollution and abuse; the key to finding cures to animal and human disease.

The microbiome is the "interferometer" between the environment and the living organism. It allows the organism to exchange nutrients and waste products with the environment. It allows the organism to defend itself as needed and fundamentally exist on this earth.

It is important to understand that it is always in balance. Now that balance may not be what we want for our or our animal's health, but Nature has an arbitrary cause and effect operational mechanism. Understand that when we put in an antibiotic, the result is then balance for the alteration we have induced. Yes, it is out of balance from what we need to be healthy, nonetheless, balance for the consequence resulting after the antibiotic does its job.

Enderlein and others - competitors of Pasteur - proposed that the terrain was superior to the inhabitants and, in fact, the terrain determines the inhabitant. The use of antibiotics and subsequent antibiotic resistance bears this out. With the use of antibiotics, one is changing the terrain.

The fundamental terrain characteristic is nutrition: vitamins, minerals, atmosphere, temperature, moisture. Regardless what probiotic inoculation we place in any environment, the characteristics of the terrain determine what lives and dies.

If we look at geological succession from bare volcanic rock to mature forest, we see an evolution from simple initial bacteria all the way out to thousands of species of bacteria, fungi, protozoa and micro-arthropods. Anything we do, interventionally from chemicals, nutrients, physical disturbance, will determine the subsequent characteristic of the microbiome and, subsequently the living multicellular organisms dependent upon that microbiome.

This ties the soil and agriculture to human health. The status of the soil and its microbiome determine the nutrient density and quality of the food harvested from the soil. This food determines the nutrient mix feeding our and our animals' microbiomes and, thus our/their health. This understanding allows us to grasp the work of Steiner - energetics of all things, Chaubaussou - who proved insects only attack sick plants, Callahan - who proved the mechanism by which insects differentiate sick from healthy plants, Huber who furthered the specifics on disease specific nutrient imbalances.

We will cover many different adverse microbiome agents from pesticides including glyphosate to industrial chemicals, nuclear radiation to toxic metals, fertilizer salts to urinary excreted drugs and antibiologics. All alter the terrain and, thus the microbiome. Most fundamentally function at the molecular level with some form of chelation of trace elements - nutrient interference.

Once we know and understand the big picture connection of all life and then how various individual products alter the terrain and subsequent microbiome; we can formulate corrective actions, all of which must begin with better nutrition from the soil to human health. There certainly will be stop-gap emergent measures needed as the various eco-systems transition from sick or near dead to healthy and progressive. This is negative entropy.

Just as we must understand algebra to get to calculous to get to engineering, we must understand basic sciences to get to connecting the soil to human health and everything in between. It is really not so complex to grasp or to fix from a scientific perspective as it is from a cultural, industrial and leisures of life perspective.

With all this said, it is important to acknowledge all the elephants in the room. Environmentally we have major dead zones at the mouth of all major rivers due to agricultural fertilizer, pesticide and animal waste run-off, industrial chemicals and municipal waste including every drug and synthetic hormone consumed by society. We have destroyed or severely damaged most of the major reefs around the world with these pollutants leaving our shores more susceptible to hurricane damage, severely reduced seafood spawns and limited fishery harvests.

We continue to destroy the rain forests in the name of agriculture and logging, both in unsustainable and toxic ways. The weed killer glyphosate, has become the number one herbicide sprayed around the world creating not only rampant weed herbicide resistance, but also adversely altering the soil and animal microbiome, contributing to endocrine disruption in the amphibian, animal and human population, directly causing cancer and birth defects especially in the poorest communities least protected from such assault.

We have created an agriculture that is so dependent upon toxic chemistry that farming has developed into one of the most toxic and hazardous professions in the world. This “agriculture” has created a nutrient deficient, tasteless fake “food” system at the foundation of the most unhealthy dietary approach on earth, the Standard American Diet. The mantra created from this designed decline is that we must genetically engineer our crops in order to feed the world, the ultimate lie to convince the consuming public that genetically engineered food is both necessary, appropriate and safe. It is none of these and the antithesis of biological science.

We have created an environment where precocious puberty, teenage female cancers and premature ovarian failure are not only common, but the norm in many areas; where hypospadias, undefended testicles and hypogonadism are the norm; where birth defects and gender dysphoria are nearly expected; where teenage suicide, ADD, autism, bi-polar disorder, OCD, ODD and allergies are the norm, over 30% of children are drugged, childhood cancer is the fastest growing age group for cancer and this generation is the first expected to under live its parents. We ignore the junk diets, contaminated vaccines, drugs, convenience procedures - prenatal ultrasound - pesticides, industrial chemicals, stray currents and radio wave pollutants, synthetic hormones, dirty water, artificial sweeteners and so forth that begin in-utero and critical post-natal period of human and animal development because “industrial science” has approved them.

We have developed a medical system where though we have, undoubtedly the premier emergency medical system in the world, we are rated at 37th in the world for overall health, 11 out of 11 of the 11 wealthiest countries; have one of the worse infant mortality rate of these countries, 33/36 (OECD) Organization for Economic Cooperation and Development countries, and, yet spend nearly twice per person what any other country spends.

We are told that new drug development and life-saving procedure development occurs in the US long before they are available to other countries, yet these “truths” only translate into more cost, poorer citizen health, more environmental decline. The US medical system is the 3rd, yes 3rd leading cause of death behind heart disease and cancer. Medical research is designed to produce profits, not “cure” and results directly in human experimentation and death all in the name of acceptable collateral damage and the “greater good.”

A fine mess we have made of health of every living thing on this planet, which we have spread around the world in the name of quarterly profit numbers. It is fixable and like any repair project from the simplest tool to the most complex computer, we must first identify all the problems, their causes and fundamental processes. We can then get to work, as many are around the world, in a collective effort to reverse the damage and regenerate all sustainable life.

The fix starts with understanding nutrition and then applying it to diet and supplementation from the soil to the human consumer. Therapeutic nutrition is what will heal the microbiome and its hosts, taking the first major step in changing the mind-set of the chemical-industrial consumer; that is to eliminate the perceived “need” for chemical/drug intervention by reversing or preventing, in the first place, all the “diagnoses” given to justify chemical/drug intervention; everything from insect pest and disease organism infestation of crops to autism, ADD, hypogonadism, cancer, autoimmune diseases and so forth in the human population.

The consumer reigns supreme. Regardless what industry and governments dictate, the consumer votes daily with his/her dollars, pesos, yen, pounds, euros, liras, dachas, etc. We change agriculture both with better food and consumer demand/purchases. As consumers change their purchases/demand, this forces agriculture/agribusiness to change itself.

Fall Symposium at Bard College September 19-20, 2019

Martha Carlin, Citizen Scientist, CEO/Founder, The BioCollective, LLC

The human body and the planet are complex ecosystems, yet the last 100 years or so of research in science and training in medicine have become increasingly reductionist. This is partly because we have developed better and better tools to looking at smaller and smaller parts of the complex system. These tools have enabled us to have tremendous knowledge about the smallest parts of our complex systems. Yet, this ability has taken western civilization further away from the understanding of the interconnectedness in the system. Science and medicine has become so specialized that it has become increasingly difficult to keep up with research in one's own field, let alone those in other specialties. The practice of "General" medicine or "General Knowledge" [liberal arts] has gone out of fashion. But the generalist is often the more creative and imaginative problem solver.

Our planet is a complex ecosystem within an even larger complex solar system. It is not possible to sufficiently separate ourselves or any single organism, cell, particle or event from everything else in the system. Quantum physics has shown us this. Everything is connected. Our health and environmental problems have grown increasingly complex, even as our approach to trying to solve them has grown increasingly reductionist. The importance of shifting our thinking to a more complex, systems based approach cannot be understated if we are to solve these complex problems.

Some Key Principles of Systems thinking

1. **Everything is interconnected:** We live on a closed ecosystem called planet Earth where everything is connected to everything else. Otherwise, it ceases to survive and thrive. What we do to the planet (air, water, land) we do to ourselves.
2. **The easy way out often leads back in:** If the solution were easy then it should have already been found. If it sounds too good to be true, it probably isn't.
3. **Today's problems are yesterday's solutions:** We need to make sure we don't accidentally create tomorrow's problems through today's solutions. The Bard Symposium will provide insights into many of yesterday's solutions that have become the sources of major health and environmental problems today.
4. **There is no blame in complex systems:** Everything is interconnected. Thus, it's impossible to ever find one culprit for a problem. Systems have both the issue and the solution embedded within. Trying to find a single cause for any single problem presents and easy excuse to say that X did not cause Y. Thinking in systems allows us to begin to understand that A plus B plus X, may be causing Z providing an approach that doesn't let contributors off the hook for not being THE single cause. Understanding synergistic effects is an important framework for understanding. It should also help us think about how our safety testing frameworks have been established and implemented and may not serve the intended purpose of protecting us and our planet.
5. **Parts are elements of a complex whole:** Everything is part of something else; there are no isolated elements in a complex system. What we do "outside" to our environment, we do to ourselves. We are not separate from our environment. And we are constantly communicating with our environment and everything in it.
6. **There are no simple solutions to complex problems:** We need to embrace complexity in order to truly address complex issues. Otherwise, we just deflect the problem to somewhere else in the system, like the balloon that is squeeze from one end and creates a bulge on the other side.

7. **Small, well-placed interventions can have big impacts:** A well-designed, small intervention can result in significant and enduring systems change if it is in the right place – this is called a leverage point. Restoring wolves to Yellowstone Park is an example of how a small intervention can have dramatic impacts in reestablishing an ecosystem in balance.
8. **Humans make linear systems – nature makes non-linear, circular ones:** We can learn to create regenerative products and services through understanding nature's design principles. Microorganisms can make, as well as breakdown many substances. This is just one example of non-linear systems in nature. In natural systems there is no waste. Humans have created linear systems that produce a tremendous amount of waste.
9. **Time changes complexity:** Over time, things naturally get more complex. Simplicity and efficiency are very different things, yet we always think we can oversimplify complexity or reduce it down to the sum of its parts. Nature is synergistic. In nature, time will breakdown parts of the system to create something new – without waste.
10. **'Failure' is discovery in disguise:** If we are not afraid to fail and learn, then we have a much greater chance of finding helpful approaches. Fear of failure reinforces old behaviors that are not working. Don't be afraid to try something new, unusual, completely out of the box.
11. **Cause and effect are seldom related in time nor space:** There is a mismatch and often a delay in the relationship between the cause of a problem in complex systems and the result (or symptom) appearing obvious. We need to reestablish and fine tune our long term observational and computational methods to better understand this long view and the synergies within the system. For example, the repeated exposure to certain oral antibiotics early in life can select for a particular microbiome ecosystem that over the long term will drive disease rather than health. The system is complex and these impacts will not be immediately obvious. As such the connections are missed in analysis, research and medicine.

The Human Microbiome is a system within a system within a system….. like a Russian nesting doll. It is a useful framework and through technology and AI can provide a map to the interconnected network between Humans and their environment.

Restoring and Protecting the Human Superorganism

Rodney Dietert, Professor Emeritus, Cornell University (rrd1@cornell.edu)

Were you taught that humans represent a single species among many on earth? We are not and never were. At our core, we are an epic, composite superorganism made up of thousands of species that occupy numerous sites within and on the human body. We are like a walking version of a coral reef as described in *The Human Superorganism*. Almost all of our species are microbial as are more than 99% of our genes. Our microbes and their genes are referred to as our "microbiome."

The 21st century view of humans as a superorganism is hardly shocking when you take a look at life on Planet Earth. Microbes are the predominate life form. All of earth's complex animals and plants have their own specific microbial partners. But microbiomes also exist in earth's media: soil, air, and water. We live in a sea of microbes that connects what is inside us with that which is beyond our bodies. It is a continuum where the microbes on and in us communicate both with our human mammalian cells as well as with the microbes outside of our body. Our microbes make us whole. We cannot thrive or even survive without them because we were designed to partner with them. Our microbes drive our development, metabolism, and physiology. Lose enough microbes, and we become sick, sleepless, depressed, mentally impaired, and increasingly disconnected from each other as well as other life on earth.

Our ancestors had an intimate geographic relationship with the food they consumed, the soil in which it grew or was raised, and the microbes that supported the soil, plants and animals within their local community. These ancestors had a robust diversity of microbes within their bodies and their environment that enabled them to be whole and to thrive. We have lost much of that microbial diversity and function today. Destruction of the microbiome is a leading cause of the ongoing chronic disease epidemic; additionally, it contributes to an increased susceptibility to infectious diseases through a loss of what is known as colonization resistance. Our immune system develops in concert with our microbiome. Immune cells are trained by our microbial co-partners. If that co-development is removed or hampered, we are destined for later-life inflammatory-driven, chronic disease, which is precisely the epidemic we see today.

What happened? Our food changed. We are awash in herbicides (*e.g.,* glyphosate). We take more drugs than ever to treat an ever-increasing number of managed, but rarely cured, medical conditions. Increasingly, we congregate into urban megacities that are microbial wastelands. These destroy rather than enrich our microbiomes.

Whether by design or via a lack of biological understanding, we made decades of decisions regarding food, drugs, medicine, environmental chemicals, and lifestyle that each contributed to an eroding of the human as well as other microbiomes. Even the way we go about determining the safety of our drugs and chemicals has ignored the microbiome and failed to protect the human superorganism. It is time to recognize what we are at our core and to act accordingly.

These are the topics I will discuss at the 2019 Bard Symposium.

Bard Reimagining Human Health Symposium by Art Dunham DVM

If 45 years of large animal veterinary medicine has taught me anything, it is the value of excellent animal husbandry and nutrition. If animals are well cared for and if they are fed correctly, practically any veterinary program works, but if the two are not adequate, practically any veterinary program will fail. (An ounce of prevention is worth a pound of cure.) Many times, today's human medicine and veterinary medicine forget this. Blaming genetics or some new disease entity and coming up with another shot or pill is easier than changing environment and diet. Doing so also makes money for those selling products. After the introduction of Round-Up Ready soybeans in 1996 and of Round-Up Ready corn in 1998, questions about the health effects of glyphosate use put me in contact with a group of plant pathologists, soil scientists, crop consultants, biological farmers, nutritionists, and human medical doctors. The knowledge gained from this group further solidified my view that environmental-soil health, plant health, animal health, and human health are all inevitably linked. Among the relationships, good soil health is a requirement at the beginning and end of the circle of life.

I am a clinician and not a researcher. If I consistently make observations that do not seem to match current veterinary science, I do not immediately give up on the observations, but do a more complete search for science that will hopefully back my point of view. I have way more questions than answers. Because of world -wide lack of public funding, many important questions are not being asked or answered. (During the 1960s, the USA spent 2% of its tax dollars on public research while now that amount is under .7%.) Our FDA recently detected a stray gene in genetically engineered polled cattle that caught the developers in complete surprise. Thank goodness our FDA still has some labs. Our EPA does not have the labs it had.

Now that we have mapped the genomes of many plants and animals along with bacteria and viruses, we realize that one gene does not code for only one protein and that what we thought was junk DNA is not. We also know that we share 40% of our mammalian genome with plants and 60% with insects. This means that the metabolic systems directed by these shared genes are identical as well. This should make it imperative to do long term epigenetic studies before approving new herbicides and insecticides and combinations. We are just dabbling in epigenetics and are not that much more advanced in studying GI microbiomes or the symbiotic mycorrhizal community of many plants. Because of this we need regulation and the use of the precautionary principle. We need more agroecology and less reliance on chemistry. (How do we change course when over 60% of the world's seeds are now owned by 4 chemical firms?)

Below is a very incomplete history of some of my comings and goings before this conference.

1996 Round Up Ready soybeans introduced by Monsanto

1998 Round Up Ready corn introduced by Monsanto

2002 I started to question the increasing glyphosate use since it seemed that a few of our most profitable cow-calf and swine clients that did not adopt the technology had more success raising livestock trouble free than those that did adopt.

2002 Due to losing market share, Pioneer-Dupont paid royalty to Monsanto and introduced their RR soybean. Because of safety concerns, they added another gene to start the breakdown of glyphosate in the GMO plant. This alteration eventually resulted in a lawsuit since Monsanto said the royalty paid did not give Dupont the right to change the GMO which was fine the way it was. The results of that suit were never shared with the public.

2004-2005 Confirmed Mn++ deficiency in “pea” (small) ovary heifers, gilts, and sows. Also confirmed Mn++ deficiency in stillborn and weak deformed calves.

2007 Phoned Dr. Don Huber after reading his article in the “John Deere Furrow” about the need to foliar fertilize RR beans after Round Up application with Mn++ and Zn++. This is most necessary on sandy high PH soils like those found in our practice area.

2009 Met Dr. Don Huber for the first time at an agronomy meeting in Amana, Iowa. He was becoming a main mentor and still is.

2010 Talked to a closed- door meeting of the science committee of the Iowa Corn Growers Association with agronomist Bob Streit and plant geneticist and crop consultant Dr. Mike McNeill about the health effects of Fusarium mycotoxins in hog and cattle feed. Glyphosate use favors the Fusarium mold family and is a risk factor for increases in Fusarium mycotoxins as shown by ARS scientist Dr. Bob Kremer and others.

20? Went to a think tank organized by Dr. Arden Anderson in Florida. Much discussion about citrus greening and glyphosate’s role in it.

20? Responded to Canadian swine consultant Dr. Mike Sheridan’s question on the ASSV-L about squatter pigs due to demyelination of the spinal cord from B12 deficiency. When his clients went back to using small grains in both the pig and sow rations that were not spray dried with glyphosate, the problem disappeared. (Glyphosate likes Co++ about 100X more than Mn++.)

2013 Contributed to my daughter’s book America’s Two-Headed Pig Treating Nutritional Deficiencies and Disease in a Genetically Modified, Antibiotic Resistant and Pesticide Dependent World, by Leah Dunham

2014 Went to the Second Annual Food Safety Summit in Beijing, China. Ate breakfast with Dr. Monika Krueger. She has PhDs in microbiology, mycobiology, and veterinary pathology and spent much of her career as a human health researcher in Leipzig, Germany, with major emphasis on sudden infant death syndrome. I learned more about toxicoinfectious botulism from her than I did through all my other searching. I still want to get her 7 Elisa test kits for BoNt on this side of the Atlantic.

2015 Started to see Cu++ deficiency in sheep and goats. Amish clients using non- RR corn need to add less Cu++ to their mineral than clients using RR corn.

2016 Went to the Monsanto Tribunal at the Hague and then went on a farm tour with host agronomist Ralph Havinga. We went to 2 dairies that had cows drinking like cats and showing signs of toxicoinfectious botulism like I had seen in 4 herds in our practice. The next day of the tour was cancelled and we went back to one of the two dairies and I addressed dairymen, veterinarians, and regulatory people with Ralph translating into Dutch. Germany had outlawed all spray drying of non- RR crops with glyphosate some years before partly because it is harder to brew beer with barley spray dried this way. The Danes had voluntarily quit until a few weeks before I was in Holland in late October, when they decided to leave the handling of that fall’s crop up to individual producers. Both the dairies I visited were getting wet brewers from a Danish plant where many of the producers were again spraying their barley and luckily it was a plant where Monika Krueger along with pork producer Ib Pedersen were monitoring glyphosate levels. One of the dairymen attending my presentation had lost 30 cows diagnosed with pneumonia at the vet school during the previous week. The aspiration pneumonia was secondary to botulism. Glyphosate at very low levels can kill beneficials that hold down Clostridia and the BoNt some of them can produce while at the same time it takes a very high level to kill Clostridia. The Netherlands have now joined Germany in outlawing all spray drying of non-RR crops with glyphosate. What is wrong with the USA and Canada?

2017 Went to the Glyphosate Round Table at the Calgary vet school organized because of the efforts of Dr. Ted Dupmeier. Monsanto was invited and participated but did not put up much rebuttal.

Here is part of the presentation:

You cannot tackle the risk factors of glyphosate use in Mother Nature's world in a few minutes. This topic is a complicated ecological issue that more than likely includes antimicrobial resistance.

Anyone evaluating glyphosate should know about all 3 of its patents: 1964 as a general chelator or metal cation binder to clean up metal boilers and pipes, 1974 as a herbicide, and 2010 as a human parasite control agent and antimicrobial.[1] All 3 of these patents depend in part on glyphosate's ability to bind with trace mineral cations that are necessary cofactors in biological enzyme systems. Log of chelation formation constants (K values for glyphosate and some cations) are: Cu^{++} 11.93, Zn^{++}8.74, Ni^{++}8.10, Cd^{++}7.29, Co^{++}7.23, Fe^{++}6.87, Mn^{++}5.47, Mg^{++}3.31, and Ca^{++}3.25.[2] Industry wants everyone to ignore the first and last patent even though they are as accurate as the 1974 patent. After glyphosate is used as a herbicide or as a drying agent on non-GMO crops, it does not wrap itself in Velcro to prevent chelation and antimicrobial effects. Our present available science has trouble distinguishing between bound and available trace minerals in plant or animal tissue. When chelated, glyphosate loses its effects, but desorption by phosphate fertilizers can free it again (½ life is rarely 2-3 months and can be over 11 years). [3,4] Because of this desorption there are a lot more acres of RR canola around Calgary instead of the non-RR small grains, lentils and peas that used to be raised there. Will oxidative phosphorylation in a mammal provide phosphate to free it up in a mammal????

Now for the possible or probable antibiotic resistance role:

USPTO Patent Full-Text and Image Database United States Patent 7771736

Claims 6, 7, and 8 are for use in humans both IV or administered orally

Susceptible pathogens include Plasmodium that causes malaria, Neisseria gonorrhoeae, all species of the Family Enterobacteriaceae, Staph aureus, and many others.

Dosage: Generally a dosage of as little as about 1-2 mg/kg of body weight is suitable…some pathogens require a much higher dose.[5] (Standard spray dose of 1 quart per acre is 1# of glyphosate so if that is compared to the top 3 inches of soil with 1 million # per acre---that would be 1mg/kg or 1ppm. Glyphosate is a contact killer so the denominator should be the dry weight of the crop and weeds being sprayed instead of the soil where about 1/3 of the product will end up when used in the spring.)

If a doctor prescribes an antibiotic such as Cipro or a cephalosporin, we know that we should not put any unused antibiotic down the drain. The Second Annual Meeting on Antimicrobial Resistance hosted by the NIAA in 2012 in Columbus, Ohio, was devoted entirely to the role of environmental contamination. While attending the conference, I learned that that year, we used about 3X more glyphosate for ag on a Kg basis applying it indiscriminately to millions of acres than all other antibiotics put together on livestock in all forms. Before her retirement, Dr. Monika Krueger determined that if a

Staph aureus was resistant to glyphosate in the lab, it was usually a MRSA as well.[6] Gluten intolerance is more than likely first triggered by the GI dysbiosis-leaky gut due to the antimicrobial glyphosate that the wheat is commonly spray dried with rather than the gluten. Casein in milk is antigenically similar to gluten so about 80% of those that get gluten intolerance also become intolerant of dairy products.[7]

In my eyes, trying to tackle the possible antimicrobial resistance caused by animal agriculture without including glyphosate in the discussion, looks like mighty poor science.

Foot notes: [1]United States Patent #7771736 put USPTO.GOV in your address box to get to the patent website. [2]Anthony Samsel, Samsel Environmental and Public Health Services, P.O. Box 131, Deerfield, NH. 03037. [3]Glyphosate degradation as a soil health indicator for heavy metal polluted soils page 5 Soil Biology and Biochemistry 37 1303-1307 (2005) www.elsevier.com/locate/soilbio S. A. E. Kools et. al. [4]Phytotoxicity of glyphosate soil residues re-mobilized by phosphate fertilization. Plant Soil 315:2-11. DOI10,1007/s11104-010-0689-3. Bott S. et.al. [5]Glyphosate suppresses the antagonistic effect of Enterococcus spp. On Clostridium botulinum Monika Kruger et. al. Anaerobe Journal homepage: www.elsevier.com/locate/anerobe Feb. 6, 2013, [6]Personal communication with Dr. Krueger. [7]Dr. Terry Wahls MD, The Wahls Protocol.

2018 Dr. Bob Kremer and a landlord in our practice area got a SARE grant to show that it is easier to raise organic matter with non-GMO-RR than with it. If every farmer in the world would raise their soil organic matter by 2% it would store an amount of carbon equivalent to all the CO2 generated by mankind in the last 100 years (Francis Thicke PhD). We could and should do much better than a 2 % increase in the Midwest but we will not do it with RR and glyphosate where ISU agronomy professors make excuses for Iowa corn and soybean farmers when they say that even with cover crop they can only raise their organic matter by .1% a year. With non-RR corn, organic matter can be raised up to .5% a year just by photosynthesis with the plant sending the right sugars and proteins to the community below. If we raised organic matter, we would also store water and hold nitrogen much better. Let's have farm policy that rewards those that raise organic matter and get rid of the long-term policy that has made small grains and hay subtract from corn base.

Symposium. Reimagining Human Health: The Microbiome, Farming, and Medicine

Blithewood Mansion, Bard College, Red Hook, NY September 19-20, 2019

Impacts of glyphosate on soil, crop, and environmental health

Don M. Huber, Professor Emeritus, Purdue University

Agriculture is the management of the ecology to optimize conditions for the production of an abundance of safe, nutritious and affordable food and fiber. Mankind has been doing this management for thousands of years using such tools as regulating water, tillage, seed selection, fertilization, crop rotation and other techniques. The ready access to chemical tools after World War II simplified some of the management decisions for weed, insect and disease control; but created a dependence on the 'silver bullet' approach of industrial agriculture at the expense of ecological management necessary for sustainability. Forty-five years ago, U.S. agriculture started a conversion to a monochemical herbicide program focused around glyphosate (Roundup®). The near simultaneous shift from conventional tillage to minimum or no-tillage, along with the later development of genetically modified crops (soybeans, canola, corn, cotton, alfalfa) tolerant to glyphosate (and propaganda on safety), stimulated this conversion and has resulted in the extensive, indiscriminant use of glyphosate for vegetation control.

Glyphosate (N-(phosphonomethyl)glycine) is a strong metal chelator that attaches to and ties up essential mineral nutrients (calcium, cobalt, copper, iron, manganese, magnesium, molybdenum, nickel, zinc) essential for physiological processes in soil, plants and animals; and, as a powerful antibiotic toxic to beneficial microorganisms in the soil and GI track of animals essential for nutrient availability and absorption; it hinders growth, vitamin production, immunity, and defense against stress and disease. Primary emphasis in understanding glyphosate's herbicidal activity has been on its inhibition of the EPSPS enzyme (5-enolpyruvylshikimate-3-phosphate synthase) at the start of the Shikimate physiological pathway for secondary metabolism. There actually are various enzymes requiring mineral co-factors for function in the Shikimate and other metabolic pathways that are immobilized by glyphosate (Co, Cu, Fe, Mg, Mn, Ni). By inhibiting the Shikimate and other metabolic pathways, plants become highly susceptible to environmental stresses such as excess or deficient water, temperature, pH etc. as well as susceptible to ubiquitous soilborne disease organisms (pathogens). It is this glyphosate-induced susceptibility to disease that actually kills the plants (weeds).

Glyphosate's antibiotic activity is toxic to beneficial soil, plant and animal microbiomes so that the microbiological balance is dramatically changed to suppress beneficial organisms that would normally be involved in physiological functions for growth, hormone production, immunity and disease suppression. In return, disease and toxin-producing organisms resistant to glyphosate are favored. This soil, plant, and animal dysbiosis (disruption) has resulted in the deterioration of soil health and fertility so that many chronic plant and animal diseases are approaching epidemic proportions. Glyphosate is a highly water-soluble, systemic compound that persists in soil and water, and is in every plant and animal cell exposed to it. As a synthetic amino acid, it is persistent in the environment and may also be incorporated into some proteins that are the building blocks of plant and animal tissues.

Plants genetically engineered for glyphosate tolerance contain the Roundup Ready® genes that provide an alternate EPSPS pathway (EPSPS-II) that is not blocked by glyphosate. The purpose of these genes is to provide herbicidal selectivity so that this systemic pesticide can be applied directly to these plants. There is nothing in the herbicide tolerant, genetically engineered plant that does anything to the glyphosate that is applied to it. It is still a strong mineral chelator to reduce nutrient density in food and feed, toxic antibiotic to many beneficial microorganisms and a persistent synthetic amino acid. The wide-spread adoption of Roundup tolerance in soybeans, cotton, corn, canola, and alfalfa has resulted in a 5 to 15 fold increase of residual glyphosate in water, food, feed, and soil. Weeds have developed resistance to glyphosate so that much higher rates and multiple pesticides are now required to maintain crop productivity. The environmental impact of the indiscriminate use of glyphosate has resulted in a reemergence of old, and the development of new plant, animal, and human diseases.

Some questions

1. What is unique about glyphosate that makes it an environmental hazard?
2. What has changed nutritionally? What happened to the 'old normal?'
3. How can damage to the soil, plant and animal microbiomes be repaired?
4. Can the deterioration in soil, plant, animal and human health be attributed to glyphosate or should other factors also be considered?
5. Can the world's growing population be fed nutritionally without glyphosate?

A One Health Perspective on Antimicrobial Resistance

Laura H. Kahn, MD, MPH, MPP

Summary

One Health is the concept that human, animal, and environmental health are linked. This concept provides a useful framework for examining and addressing complex subjects such as antimicrobial resistance and food security.

Antibiotics are the foundation of modern medicine, and agriculture is the foundation of civilization. Both are needed for an advanced society. Both are in jeopardy.

Antibiotic overuse and misuse in medicine and agriculture has resulted in worsening antimicrobial resistance (i.e. bacteria resistant to our most powerful medications). Simple bacterial infections are becoming untreatable and sometimes fatal, again. Without safe and effective antibiotics, many of the treatments that we take for granted such as elective surgeries, cancer chemotherapies, and immunosuppressive therapies become too dangerous to do because the risk for infection becomes too high.

In addition to saving lives; however, antibiotics themselves pose health threats. Analogous to pesticides, antibiotics indiscriminately kill both beneficial and harmful bugs. We are learning that the microbes that live in us and on us, our microbiomes, are as important to our health and well-being as any organ. Disruptions to our microbiomes can lead to disease.

While agriculture provides food security (i.e. the prevention of hunger), it also causes environmental degradation, environmental contamination, and ecosystem destruction. To understand climate change, we must examine a timeline of the temperature of the planet since the beginning of complex life. After early hominids appeared in the fossil record around 5 million years ago, the planet began cooling into the Ice Age during the Pleistocene era. Agriculture did not develop then for the simple reason that the planet was too cold. Much of it was covered with glaciers.

The planet's climate began to warm during the early Holocene era. With warming temperatures, humans developed agriculture which provided a relatively stable food supply. Indeed, during the entire Holocene era, over the past 10,000 years, the planet's temperature has been remarkably stable and relatively mild allowing civilization to flourish. There have been a few exceptions such as the Little Ice Age which occurred during the 16th to 19th centuries.

During the Little Ice Age, the climate deviated about 2 degrees below the Holocene baseline resulting in much colder temperatures, severe weather, crop failures, famine, and wars. Artists living during the Little Ice Age documented what the world looked like in their paintings. According to Philipp Blom, author of Nature's Mutiny, witch trials and burnings typically increased after severe weather and crop failures during the Little Ice Age because somebody, typically poor, elderly women, had to be blamed for the famines.

Agriculture is both threatened by and contributes to climate change. According to the U.S. Environmental Protection Agency, in 2017, agriculture was responsible for about 9 percent of U.S. greenhouse gas emissions. In particular, cattle in the beef and dairy industries produce about 27 percent of the U.S. methane emissions from enteric fermentation. Microbes in cattles' rumens, special

chambers of their stomachs, produce methane from the animals' feed. They subsequently burp methane into the atmosphere. Methane is about 30 times more potent as a greenhouse gas at trapping the sun's heat in the Earth's atmosphere than carbon dioxide.

Thanks to widespread greenhouse gas emissions (i.e. carbon dioxide, methane, and nitrous oxide) the planet's temperature is deviating about 1 degree above the Holocene baseline. So climate change means the change from the Holocene baseline that has allowed agriculture, food security, and civilization to exist.

The World Bank did modeling of estimated agricultural yields in 2050, assuming current agricultural practices, crop varieties, and elevated temperatures. They estimate that much of the world is going to become too hot and dry to grow food. We are already beginning to witness the effects of global warming as crops in some parts of the world are failing, and people are fleeing their homes for more habitable regions. Our goal must be to keep the planet's temperature as close to the Holocene baseline as possible to ensure the continuation of agriculture and civilization. We must curtail our greenhouse gas emissions to leave a habitable planet for our children and grandchildren.

So the question we must ask: Can we have our pork chops and antibiotics, too?

We live in a microbial world. We need to work with Nature, not against it. Currently, we are working against Nature, and we are losing.

Humans and their domesticated animals constitute about 96 to 98 percent of the total terrestrial mammalian biomass on Earth. Over 7 billion humans and almost 30 billion food animals produce a lot of manure annually, about 4 trillion kilograms of it. That's enough manure to fill over 1.6 million Olympic-sized swimming pools each year. It's got to go somewhere. Typically, it's used as fertilizer which leads to contaminated soils, waterways, and crops. Contaminated waterways and crops result in waterborne and foodborne illnesses, ultimately contributing to increased antibiotic use and worsening antimicrobial resistance.

Microbes in manure also emit methane and nitrous oxide into the atmosphere. Nitrous oxide stays in the atmosphere for a century and is 300 times more potent than carbon dioxide in trapping the sun's heat.

We don't know which microbes live in the soil since most cannot be cultured in laboratories. To get around this problem, scientists very cleverly extracted DNA directly from the soil to see what was living there. They didn't know which microbes contributed to the extracted DNA, but nevertheless, they made some unexpected discoveries. They found antibiotic resistant genes everywhere: in the Arctic, the Antarctic, in areas not exposed to human antibiotic use. It appears that antibiotic resistant genes are ancient and ubiquitous around the world.

For a long time, scientists thought that microbes used antibiotics as a form of chemical warfare against each other. That thinking was wrong. Instead, it appears that microbes use minute amounts of antibiotics, chemicals, as forms of communication with each other. Our widespread use of antibiotics has been changing the planet's microbiome. Bacteria are sharing antibiotic resistance genes with other bacteria, sometimes with other species of bacteria, to protect each other from our inundation of antibiotics into their environment. They're cooperating with each other a lot faster than we can develop new antibiotics.

To work with Nature, we need to turn to the natural foes of bacteria: bacteriophages. They have been used as anti-bacterials for almost a century at the Eliava Institute in Tblisi, Georgia. Western countries lost interest in them when antibiotics became available because antibiotics were much easier to use. But with worsening antimicrobial resistance, interest in bacteriophages has returned. The technology used to isolate them is about a century old, so much more research and development must be done before they can be widely used in clinical medicine.

Unlike broad-spectrum antibiotics, bacteriophages are highly specific. They must be identified and matched to the bacteria causing disease. Their use would be akin to personalized cancer treatments, tailored for each individual patient. For example, Dr. Stephanie Strathdee's use of bacteriophages to save her husband's life has been a game changer in clinical medicine. As a result of her efforts, UC San Diego recently established the first Center for Innovative Phage Applications and Therapeutics in the U.S. Her book, The Perfect Predator, describes her experience.

Ultimately, we must maintain our ability to treat bacterial infections and to sustainably cultivate safe and nutritious food if we want to live in an advanced civilization. We must do this on a hotter, drier, stormier planet. A One Health approach linking human, animal, and environmental health will be essential.

Fall Symposium at Bard College September 19-20, 2019

David L. Lewis, Ph.D., former EPA research microbiologist, author of *Science for Sale*

Until Congress passed the Clean Water Act of 1972, the solution to pollution was dilution. Lead, mercury, arsenic, pesticides, pharmaceuticals and other hazardous chemical and biological wastes were piped into rivers, and settled out in the bottoms of the oceans. In accordance with the Clean Water Act, President Carter created wastewater treatment plants in every municipality. Now, the most dangerous pollutants, including heavy metals and fat-soluble toxic organic chemicals, settle out with sewage sludges in large basins at wastewater treatment plants. Sewage sludges, a.k.a. biosolids, contain all of the fat-soluble pollutants found in water at millions of times higher concentrations. They also contain virulent forms of vaccine-derived viruses, including measles, mumps, rubella, rotavirus, smallpox, chickenpox, and yellow fever.

At first, sewage sludges were usually buried in landfills or dumped offshore. Then, in 1988, Congress banned ocean dumping fearing that it may generate polio epidemics. In 1993, the Clinton Administration deregulated all pollutants in sewage sludges, except nine heavy metals, in order to allow sewage sludges to be used as an inexpensive fertilizer on farms, forests, school playgrounds, athletic fields, golf courses and other private and public lands.

Scientists in EPA's Office of Research & Development (ORD) where I worked as a senior-level research microbiologist unanimously opposed land application of sewage sludges. Spending billions of dollars to remove hazardous chemical and biological wastes from water, only to spread them on soil everywhere we live, work and play defied common sense. To overcome opposition within ORD, EPA's Office of Water and the USDA worked closely with the wastewater industry to fund land grant colleges to publish research supporting the safety of land application of sewage sludges. Research that my colleagues and I in ORD and at the University of Georgia published linked land application of sewage sludges to illnesses and deaths caused by exposures to hazardous chemicals and infectious agents in sewage sludges. Recently, I also submitted an article linking sewage sludge to autism, which dramatically affects the human gut biome.

Congress held two hearings into retaliations against me by political appointees under Presidents Clinton and Bush, and passed the No Fear Act to protect federal whistleblowers. In the end, money and politics won over research that I authored in *Nature* and other leading science journals. It cost me my career as a research scientist; however, I continue to write commentaries and books on the subject, and participate on panels of experts, including, for example, at Harvard University's JFK School of Government and the Royal Society of London.