The 91% You Don't Know

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Did you know, that there are ten times as many microbial cells in a pigeon then there are host cells and 100 times as many microbial genes than there are host genes?

How is this possible? Well, in general, most all bacteria are single celled microbes ranging between 0.5 and 5 microns (μm) in size, while pigeon muscle cells may be 100's of μm in diameter and thousands of μm long. E coli cells are typically rod-shaped, and are about 2.0 μm long and 0.5 μm in diameter. Yeast cells are typically 3–4 μm in diameter, fungus 2-10 μm in diameter, while fat cells can be hundreds of μm in diameter. For reference, $1/1000^{th}$ of an inch = 25.4 μm.

As racing pigeon fanciers, we aspire to know about the muscle texture, skeletal structure, skin & feather quality, wing shape and lung function of our birds, but what do we really know about the microbes that live inside of our birds and their structure, quality and function? I suspect, very little!

Fifty years ago, this lack of knowledge about the microbes living within our birds was of little consequence to us, as we left the health of our birds, to a great extent, in the hands of nature and the natural immune response. However, over the past fifty years, this has drastically changed and the fancier of today is exposed to nearly a hundred different medications and antibiotics with which to treat their birds.

In the early 1980's, when I first became involved in the sport, my well equipped medicine cabinet consisted of Sulmet, Piperzine, Flowers of Sulphur, Emtryl and OxyTetracycline. Sulmet and Emtryl might be used three times a year; before breeding, before old birds and again before young birds. Piperzine was given twice a year. Flower of Sulphur was put on the grit in Summer when there was reports of pox outbreaks. I did not know when or how to use the Oxytetracycline correctly, but I think I probably administered it for five days, prior to the old bird and young bird race seasons.

When I got back into the sport in 2001, I was amazed at how medication usage had grown in our sport. It was recommended to me that I treat the birds on a cyclical rotation throughout the year. One week, treat for cocci, the next week treat for canker, next week salmonella / paratyphoid, next week e coli, the next week treat for respiratory. This was called the “Shotgun” approach as you did not know if the birds had a problem you just treated for everything in case they had something.

There were also specialty products that one could use to “hopefully” enhance their results. One that I had was a product to clear the mucus from the throat and nasal cavity called Bromhexine. So, whenever I was treating for respiratory I also treated with Bromhexine.

Not only was it important to rotate weekly the treatment you were using, but it was also important to have at least two different medications for each “cure”. This was because by the year 2001, many pathogens had started building resistance to the antibiotics and medications being used against them. The solution we came up with, in order to solve this problem, was to switch between different products every couple of months, in order to fool the pathogens.

For example, my respiratory treatments at different times included: L/S 50 (lincomycin / spectinomycin), Suanovil (spiramycin), and Amoxicillin.

Some fanciers, thought that it was taking to long to get through the cycle, so they started stacking cures. In order to accomplish this, they needed to reduce the days of usage for medications and antibiotics below the recommended number of days printed on the medication label. The stacking method, culminated with the development of the ever so popular three in one, four in one and five in one, all inclusive treatments.

Hopefully by now, we all know that you cannot use antibiotics as part of a preventative health program, without weakening the overall health prospects of your birds. Going back to the early 1990's, Dr. David Marx, DVM, regularly warned us in his pigeon health articles, printed monthly in the Digest; "Do not use antibiotics as a preventive. They will not work as a preventive, but will only allow the bacteria to become resistant to it, then it won't work when we really need it."

Stacking, offers an additional risk in that not only are we cycling through medications and antibiotics in a preventive routine, but we are also shortening the number of days for those treatments, guaranteeing that many of the pathogens will survive the truncated treatment period and pass resistant DNA to the next generation.

When you treat your birds with a certain antibiotic, the bacteria least able to resist die off and the bacteria most able to resist survives and becomes the seed stock for future generations. You just cannot fool "mother nature", the evolutionary mechanisms which have advanced life on this planet are superior to the mechanisms of man used to control nature.

In 1928, when Alexander Fleming accidentally discovered penicillin, a new promising era arrived. Antibiotics proved to be wonder drugs that killed bacterial infections without harming the host. Never before had nature and sickness seemed so much within the control of mankind. The euphoria was short lived however, as the bacterial world revealed its genius for becoming resistant to antibiotics.

The early advances made by antibiotic and antiviral medications seems to have been completely overcome by the continued evolution of antibiotic and antiviral resistance. By the mid-twentieth century, antibiotics had nearly wiped out tuberculosis. But by the 1990s, tuberculosis began to approach epidemic numbers again, and now kills more than 2 million people every year. This same story has been repeated time and again, as one after another antibiotic or medication loses its effectiveness to the evolutionary processes at work within the host, processes that selectively breed better suited microorganisms, resistant to the antibiotics and medications introduced into their environment.

We simply cannot accomplish long term health in our birds by employing either the cyclical "Shotgun" method or the "Stacking" method. These methods, will become less and less effective, until they are no more effective than the antibiotics we used for over half a century to combat tuberculosis.

What we need then, are mechanisms other than the use of antibiotics and medications, which can assist us in maintaining the health of our birds. Interestingly, scientists are coming to the same conclusion and are trying to develop ways to treat patients without killing the bacteria that are making them sick. If we can control the microbial populations without killing off the offending microbes, then selective breeding for resistance does not occur and the evolution of resistant strains does not occur.

Where are scientists now looking for help in controlling bacterial and viral infections? Within the microbiota of the host itself. Scientist recognize that the microbiota (the totality of bacteria and other microorganisms residing

within a host) is self controlling, and that these thousands of different bacterial strains and other microorganism (the 91% you don't know), play an important role in maintaining the health of the host.

In general, there are two important mechanisms by which microorganisms control their environment. From the host point of view, the benefit derived from bacteria living within it, is that these organisms break down the food we eat so that we can utilize the vitamins, minerals, carbohydrates, proteins, fats, etc, that we need to maintain our existence.

In performing that process, these bacteria produce certain organic acids, hydrogen peroxides, bacteriocins and other by-products that are beneficial to some microorganism and antagonistic to others. When the diversity of microorganism are in their proper populations, they exert population control over each other and maintain the health condition necessary for continuation of the host.

Another mechanism by which the microbiota controls itself, is that they work with the immune response by stimulating the production of certain "search and destroy" navy seal teams, that identify pathogenic organisms, tag them with GPS devices and send in the cruise missiles (my colorful description of this process), to eradicate the threat.

Let me give you an example of how bacteria assist the immune response and how antibiotics bungle up the whole operation and even threaten the health of the host.

Recently, researchers found that when they administered oral doses of Neomycin to mice, that these mice became more susceptible to influenza infections of the lungs. After much research, they discovered that there was a group of neomycin-sensitive bacteria, in the gastrointestinal tract, that stimulated the immune system to produce certain interleukins, and that the production of these interleukins are necessary, in order to identify the presence of certain pathogens including viral pathogens in the lungs.

Interleukins, are molecules produced by the immune system, whose primary function is to signal or communicate with other cells of the immune system. Each interleukin has a unique molecular structure that allows it to only attach to certain target molecules. When a virus invades a cell, it changes that cell in order to induce conditions advantageous for viral replication. One change is that viral glycoproteins are expressed on the surface of the infected cell. These glycoproteins are molecular chains, and on one end of the molecular chain is a terminating receptor (docking station).

Each interleukin has a corresponding protein receptor, so the Interleukin One molecule (IL-1), binds only to the Interleukin One Receptor (IL-1R). When an Influenza virus invades a host cell, it expresses viral glycoproteins on the cell's surface, terminating with the Interleukin One Receptor (IL-1R). This allows the IL-1 molecule to attach to the viral glycoprotein's IL-1R receptor and to signal the immune system that it has encountered the Influenza pathogen.

Since there are numerous pathogens that will express glycoproteins terminating with the IL-1R receptor, the IL-1 molecule is able to further differentiating the specific pathogen, by the presence of atomic "markers" within the terminating receptor strand.

Sometimes, a viral pathogen will express glycoprotein strands having more than one type of terminating receptor. In the case of the Influenza virus, it will also express viral glycoproteins terminating with the Interleukin Eighteen Receptor (IL-18R). So, when the immune system receives "marker" signals from the IL-1

and IL-18 molecules, it has enough information to initiate a specific response targeted towards the influenza virus. This response will include activation of T-cells, B-cells. NK cells and Macrophages all of which easily locate the virus infected cells because they have a GPS chip (interleukin) attached to them, signaling their location.

The treatment of the mice with Neomycin, knocked out large populations of neomycin-sensitive bacteria and the unfortunate consequence of this was a great reduction in the production of interleukin 1 and interleukin 18, which resulted in no functional early warning system to identify pathogenic influenza infections. This study, was the first to demonstrate how treating one organ of the body (the GI tract) influenced the health of another organ (the lungs).

Though pigeons are not easily susceptible to the influenza virus, they are susceptible to Rotovirus, Adenovirus, Circovirus, Herpesvirus, Paramyxovirus, Coronavirus, Poxvirus and other viruses. I can't help but wonder if we are not compromising the immune defense's ability to detect and destroy these viruses, as a result of the health programs we have developed for our birds.

There are currently 36 known interleukins, and each interleukin has different bacteria or other microbes which can stimulate the immune response to produce them, it makes me wonder just what health problems we create in our birds when we “carpet bomb” their digestive tracts with the Shotgun approach or the 3, 4 or 5 in one stacking products. Maybe we are creating a cascading effect, where the treatments we give for one health problem, becomes the trigger for the next health crisis.

A study released in July of 2012, demonstrated that interleukin 22 when present in the mucosal layer (the interior lining of the mouth, nose, eyes, ears, intestinal tract and lungs), plays a critical role in protecting the body from E. coli, pneumococcus and other bacterial infections.

Interleukin 22 in combination with a protein called HVEM, function like border guards that respond to the presence of invasive bacteria and signals the immune system to send in more troops. Without their involvement, the body would be overrun by many disease causing bacteria.

Though scientists have yet to identify the particular microorganisms which play a role in stimulating the immune system to produce Interleukin 22, they do know that specialized cells and glands within the mucosal layer are stimulated by the microbiota to secrete interleukin 22, and that the HVEM protein in conjunction with interleukin 22 are the first line of defense against bacterial infections of the respiratory and intestinal tracts.

Now, I am taking a wondrous and vastly complex system and simplifying it for this article, but in reality the innate and adaptive immune systems are responding to millions of inputs from specialized receptor cells embedded throughout the mucosal protective barrier, which sample the microbiota and report on changes in the composition of the vast diversity of microbial populations within the microbiota.

The innate and adaptive immune systems, have the ability to respond to changes in the microbiota, by producing any number of antibodies, interleukins, chemokines, interferons, macrophages, neutrophils, dendritic cells, mast cells, eosinophils, basophils, T cells, B cells, helper cells and natural killer (NK) cells. All of which can be used to regulate the populations of microbes which make up the microbiota.

The innate and adaptive immune systems, can also stimulate goblet cells, paneth cells and brunner glands throughout the mucosal layer to produce specialized secretions (mucins, defensins, lysozymes and phospholipase), released into the microbiota, to encourage the growth of some microorganisms or discourage the growth of other microorganisms.

Thousands of scientists have spent their professional lifetimes studying the immune system and the more they discover, the more they comprehend how intricately complex are the interactions and responses between the microbiota and the cells & tissues that comprise the mucosal layer.

Whether you believe in Evolution or Intelligent Design, "Nature" has developed the most successful health system on earth, without (or in spite of) the intervention of man and science. I suggest to you, that we need to bring our own loft management programs more into balance with the natural immune response and the microbiota inherent in our birds.

I consider the vast diversity of microbiota, present in both the gastrointestinal tract and the internal organs to be a treasure trove of nature's proven solutions for the problems we encounter in maintaining health in our birds.

The use of antibiotics and medications, as the mallet in a game of Whac-A-Mole, does not provide long term solutions for our sport, other than creating a cascading effect that pops up one health crisis after another, and interferes with the natural development of the internal organs, endocrine system and the immune system.

It is my belief that the current health regimes of cyclical and stacked treatments, result in increasing numbers of inferior birds, in need of constant treatment throughout the race season, whose internal organs, nervous system, endocrine system and immune system are stunted or damaged, resulting in race birds washed up after only one or two years on the program, These birds when moved over to the breeding loft, have not been raced over a long enough period of time to select for "Durable Competitive Advantage".

In very young pigeons, the microbiota plays an important role in stimulating the functional development of the intestinal tract and other organs. The microbiota also influence the development of the blood supply, the epithelial tissues and the mucosal barrier. Recent data also suggests that the microbiota plays a role in the development and function of the brain and the hypothalamic pituitary adrenal axis (HTPA), as well.

The HTPA is a complex set of influences and feedback interactions between the hypothalamus, the pituitary gland, and the adrenal glands. These influences and feedback interactions constitute a major part of the neuroendocrine system which controls reactions to stress and which regulates many bodily processes, including sexuality, digestion, immune response, energy storage and energy expenditure.

In young birds, dependence upon cyclical and stacked antibiotic and medication treatments interferes with the "natural" development of the internal organs and the nervous, endocrine and immune systems, resulting in birds deficient in many of the qualities and functionality necessary for successful racing and breeding, such as resistance to disease, a well developed navigational system, bone structures that are sufficiently hardened by proper mineralization (in order to hold up under the stresses of successive years of race schedules), and muscle tissues that will remain flexible and regenerative over many years of competitive racing.

To understand how we might breed genetically inferior birds when we utilize cyclical and stacked antibiotic and medication treatments, we can examine how Warfarin resistance developed in rat populations. Warfarin blocks the ability of the host to assimilate vitamin K, the blood clotting vitamin. When rats are fed Warfarin their blood loses the ability to clot, so then when blood vessels begin to leak, the rat bleeds out internally before the blood vessel can repair itself.

When scientist investigated how the surviving rats developed resistance to Warfarin, they discovered that these rats utilized a different enzyme pathway for vitamin K assimilation, than did the rats which died off from the Warfarin poisoning.

The surviving rat population was a small subset of the original population, whose DNA produced an alternate enzyme pathway for vitamin K assimilation, a pathway that was not disabled when ingesting Warfarin. This pathway gave these rats the ability to survive Warfarin poisoning, but at a cost. The new enzyme pathway was only $1/10^{th}$ as efficient at assimilating vitamin K, than the original pathway. The end result was that rats gained resistance to Warfarin, but those rats were genetically inferior, as they had to consume 10 times the amount of vitamin K in order to maintain blood clotting capabilities.

All antibiotics work by denying a target pathogen population access to some vitamin or mineral necessary for survival, or they work by blocking the ability of the target population to manufacture proteins necessary for survival. For example, Sulfonamides inhibit folate synthesis (folic acid) and in its absence cells will be unable to divide. Aminoglycosides work by leaving the bacterium unable to synthesize proteins vital to its growth. Penicillins work by inhibiting cell wall biosynthesis, compromising cell wall structural integrity. Gallium-based antibiotics work by denying the target population access to iron which is critical for growth.

So, whenever we utilize antibiotic and medication treatments, we are building resistance in the target pathogens in much the same manner as was discussed above concerning Warfarin resistance in rats. The surviving populations of the target pathogens have DNA which allows them to utilize less efficient pathways to overcome the effects of the antibiotic or medication. However, these surviving populations are: inefficient in converting resources, have a higher failure rate, and generate less benefit to the host, than did the original population.

Just by definition, these survivor microbes are going to have a higher failure rate, because the primary selection process is no longer guided by the evolutionary imperative, which selects for genetic material that best supports the host. Rather, in the antibiotic age, the primary selection process replicates “survivor” genetic material that best resists the effects of those antibiotics and medications pumped into the host.

The most damning aspect of antibiotic and medication usage is that they are much more broad spectrum then they are targeted, and you often end up not only compromising the efficiency of the target population but also compromising many other microbial populations which utilize the same pathways for assimilation, division and growth.

The end result is that the surviving populations of these resistant microorganisms are less able to support the host, as they consume greater amounts of resources while producing fewer benefits, and they have a higher failure rate. Through over use of antibiotics or medications, we selectively eliminate the most efficient DNA populations within the target pathogen groups while replicating the less efficient survivor populations. It is a matter of economy, we are genetically engineering the microbiota to be less efficient and less prolific.

Let's not forget, that antibiotics and medications are toxins. Giving these toxins day after day and week after week, has a cumulative effect on the functionality of the host tissues. These toxins create a heavy and destructive load on the internal organs (especially the liver, kidneys and reproductive organs), on the digestive tract, the endocrine system and even on the immune system itself.

Therefore, the cumulative effect is that many of the birds we breed today are “One and Done!” or “Two and Through!”. In response, we have simply given up on fielding race teams with a broad representation of 2, 3, 4, 5, 6, and 7 year old competitive race birds. We blame this on losses associated with cell phone towers, power lines, crop dusters, hunters, air quality, sun spots, “blue skies”, the trucker, etc., all of which, we say, leaves us with teams to small to compete across a broad spectrum of race distances.

Of course, all these seemingly legitimate reasons make us feel better about the fact that our race teams consist mainly of young birds and yearlings. However, some of us believe that “maybe”, we have just lowered the bar, that we have created a health regime whose health results give diminishing returns and that we have adjusted for this reality by breeding race birds only capable of flying shorter race schedules with less total miles, birds whose competitive usefulness is only one or two years.

Maybe the long term end result of our heavy reliance upon cyclical and stacked antibiotic and medication treatments, has produced birds with compromised internal organs, compromised immune response and down regulated microbiota selected for less efficient conversion pathways.

Maybe our reliance upon cyclical and stacked antibiotic and medication regimes, has left us with a gene pool lacking “Durable Competitive Advantage”.

So then, what can a fancier do to return “Durable Competitive Advantage” to their racing and breeding programs?

Stop trying to fool “Mother Nature”. The evolutionary process that has brought all life to our current state of existence, has proven to be a better judge of immune response and adaptation, than any program man can come up with. Therefore, you will need to find ways to depend less upon the use of cyclical and stacked antibiotic and medication programs and more upon the natural immune response and the microbiota that support it.

There are several suppliers that offer “all natural” pigeon products that support the immune system. Some of these products work by using specific antibodies and immunoglobulins to suppress the so called “bad bacteria” while encouraging the growth of the so called “good bacteria”. Some offer products which acidify the digestive tract, utilizing organic acids, fatty acids or other ingredients to create a more hostile environment for the gram negative or so called bad bacteria strains. Most of the natural alternative companies also offer probiotic / prebiotic solutions.

A very good article that should be helpful in pointing you in the right direction is “The Probiotic Dividend”. It goes into greater detail explaining how the immune system works in conjunction with the microbiota and it explains how to positively influence the immune response so that dependence upon cyclical and stacked antibiotic and medication usage decreases while the overall health of your birds increases.

As you begin to depend less upon cyclical and stacked antibiotic and medication usage, the very selection process that replicated the less efficient alternate DNA pathways will begin to favor any remaining DNA that utilized the original high efficiency pathways.

Even if some of your current microbial populations are 100% lacking the higher efficiency pathways, there is still a transfer mechanism by which your bird's microbiota may still be returned to its original composition and productivity.

Since racing pigeon fanciers allow their birds to come into contact with other race birds, some of which still carry the original or “wild state” microbial populations, it is likely that the “wild state” microorganisms with the higher efficiency pathways will to be reintroduced into the microbiota of deficient race birds, restoring the microbiota to its original or “pristine” composition and productivity.

I know some of you are thinking, “Why would you want to return pathogenic microbes to their more effective wild state DNA structures?” Remember this, antibiotics and medications paint with a much wider brush than you think, and they adversely effect many other microorganisms which are beneficial to the host.

Also, if you read the supplemental material in “The Probiotic Dividend” article, you will discover that Mother Nature, has placed these “so called” pathogenic microorganisms in the microbiota, because when in their proper populations, they assist in the health and well being of the host. That is right, bacteria like e coli, salmonella, pneumococcal, along with yeast, fungi and protozoans are all beneficial to the host, when in their proper populations.