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Zoe E. Swann

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# Cold Plasma Therapy Can One Device Change the World?

েও Written by Zoe Elisabeth Swann Illustrated by Claire Segura



he stuff of lightning bolts — plasma — changing medical industries, changing lives, versatile, and accessible. Let's jump right in.

#### Background on this New "Hot Topic"

The purpose of this article is to offer an overview of the mechanisms and potential therapeutic application of cold plasma technology. Plasma is the fourth state of matter (compare this with solid, liquid and gas). It is the most abundant state that we can observe in the universe, and examples include the sun, solar wind, lightning, and the aurora borealis.

Scientists and engineers have developed medical devices that can use plasma's high energy output to break apart atmospheric compounds and generate high concentrations of life-saving molecules right on the surface of the skin.

While the field is very young, several medical fields already use cold plasma as a non-antibiotic approach for treating infections, decreasing the risk of antibiotic resistance. Its main application is wound care, but cold plasma can combat tumor growth — and even dentists and plastic surgeons use cold plasma.

Basically, these medical devices generate reactive oxygen species which in turn react with molecules in the atmosphere. So, it turns water into hydrogen peroxide as a disinfectant, or nitrogen into nitric oxide, which is fertilizer. It has also been shown to sterilize military-grade E. coli infected water so that it becomes drinkable.

Max Planck Innovation, a technology company, described the devices as such: "Cold plasma treatment is a contact-free and painless procedure to sterilize wounds and promote wound healing. The costs are comparable to or lower than those of standard antimicrobial wound treatment."

#### The Mechanisms of Plasma

Plasma is often defined as an ionized gas containing equal concentrations of negatively and positively charged particles. As such, it is quasi-neutral, meaning that on a macro-level the molecule has an overall charge of zero, but on a much smaller level positive and negative charges contribute to small magnetic and electric fields; electrons in this excited state are very mobile and make excellent conductors. Quasi-neutrality depends on the density and pressure of the plasma. Increasing temperature and density will strip away electrons promoting positive charge. Plasma is usually very high in thermal energy, and in normal "thermal" plasma, the positive and negative particles are equally hot. However, the term "cold" or "non-thermal" plasma refers to what happens when the temperature of the electrons remains very hot, but the temperature of the positive and neutral particles is at room temperature.

New medical devices ignite the plasma for nanoseconds at a time, allowing for only partial ionization (creating a charge) of the air. The plasma and atmospheric molecules revert back to their original states after a matter of seconds. Delivering extremely local and high concentrations of hydrogen peroxide to a wound will kill bacteria and promote healing even inches underneath the skin's surface. More on that in the next section.

#### The Mechanisms of Reactive Oxygen Species

Plasma is so high-energy that it creates a "pocket" in the air by which atmospheric oxygen and nitrogen can split apart into their reactive counterparts, which quickly react with water and other molecules to form more stable molecules.

These reactive oxygen species, or free radicals, are often implicated in infection, and many people are under the impression that free radicals are harmful to the body and eat foods such as acai berries to get antioxidants. Turns out, while that is correct, it's only half the story. Free radicals actually can help the immune system fight infection. It is the imbalance in the production of free radicals and the ability of the system to detoxify with antioxidants that causes a problem. These radicals — or molecules with one or more unpaired electron its outermost shell — bind to other molecules to achieve stability, and are able to donate and accept electrons, making them extremely reactive. H2O2, hydrogen peroxide (a common household disinfectant) stimulates the production of free radicals and is a perfect intermediate product of these reactions. High levels of H2O2 activate immune cells such as monocytes and neutrophils, which then can phagocytose, or "eat" bacteria. Additionally, free radicals

Cold plasma treatment also promotes healing by increasing blood circulation in the skin, immune system stimulation, and keratinocyte proliferation – all of which are mechanisms for wound healing.

also degrade the bacteria's defense mechanism on its cell surface, further increasing therapeutic effects. Free radicals are also necessary for the production of ATP in the mitochondria — without them, cells will not have the proper energy supply.

The way in which free radicals can be harmful to the body is if they form too reactive, extremely unstable, short-lived products like OH radicals — then there isn't enough time for antioxidants to counterbalance and contain the effects. When there are just enough reactive oxygen species (ROS), they degrade bacteria. But too many, and ROS will degrade you! So H2O2 is a more stable, controlled intermediate that, when generated by these devices, will treat as opposed to harm. Cold plasma treatment also promotes healing by increasing blood circulation in the skin, immune system stimulation, and keratinocyte proliferation — all of which are mechanisms for wound healing. Cold plasma also amplifies the effects of anti-tumor agents and enzyme inhibitors, which induces apoptosis and cell cycle arrest. After just a few treatments, tumors (melanoma, glioma, GI-tract, etc.) were shown to have reduced in size.

#### The Mechanisms of Vibrations

The second important mechanism involves molecule vibrations (basically Van der Waals forces). These vibrations are necessary for protein and cellular structure and function, and on a cellular level also rely on ATP. The high energy of the plasma increases the molecular vibrations within cells, stimulating dysfunctional mitochondria, transport pumps, and ion diffusion — all vital processes within the cell. I like to think of this as jumping a car battery. Once the cell receives the boost of energy, it has a better shot of recovering.

### The Mirari

### A Cold Plasma Technology Provided by General VIBRONICS Inc.

These medical devices take several forms; the majority of cold plasma technologies out there use something that looks like a pen or a scalpel — a very fine-tipped instrument to generate and deliver plasma via an electrode to a wound or surgical incision. I recently spoke with a team who makes such a device; but they have invented a new application, which instead of using a fine point, like a scalpel, uses a large electrode array, stainless steel, and a few inches in width, that can sit on the patient's

skin and treat surface or subcutaneous wounds and diseases.

The Mirari looks a bit like a dated iPod-nano, has a single button, and has an interface that translates to multiple languages, increasing utility and accessibility. It's interesting to use — you can smell the ozone (O3), and so it's recommended to use in ten-minute intervals in a room without air circulation. The frequency of the plasma generation is within the audible range, so you can actually hear a tone while the device is on. The mesh grid generates extremely small plasma discharges evenly across its surface, initiating cascades of reactive species and their subsequent chemical reactions in the ambient air, reaching the skin and affected area via diffusion. For instance, H2O2 can be generated and, once it reaches the skin surface, it functions normally as a disinfectant, killing bacteria and aiding in immune function.

### **Public Health Implications**

Besides increased access, patient comfort, and faster health outcomes, cold plasma technology can be used in teeth whitening, sterilization of medical instruments, disinfection of contaminated water, and even as a plant fertilizer. Over the last few years, scientists have shown cold plasma to be successful as a cancer therapy in multiple types of cancer. In one 2014 study conducted by Julia Köritzer at the Ludwig Maximilian University of Munich, not only did cold plasma therapy decrease glioblastoma tumor growth and increase apoptosis, cell cycle arrest, and patient prognosis, it also restored the sensitivity of glioma cells previously resistant towards chemotherapy.

Cold plasma therapy devices are low-cost, safe, and easy to operate, making them potentially the ultimate public health tool! However, medical awareness in the U.S. is, unsurprisingly, down. There could be major economic repercussions if cold plasma technology takes off. The use of cold plasma could make antibiotics unnecessary, diminishing the entire pharmaceutical industry. It could produce clean drinking water and more efficient fertilizer. Cold plasma, the stuff of lightning bolts, can likely change the world.

# Biology

urrently, over 50 million people in the United States have been diagnosed with one or more autoimmune disease: more cases than heart disease and cancer combined. On average, autoimmune diseases take 15 years off a patient's life. Autoimmune diseases are the number two cause of chronic illness, yet the level of basic autoimmune researching funding is less than 3% of the NIH's budget. It's time this issue is taken seriously and addressed in the scientific and medical community. The first step is understanding the cause. the thymus, are also linked to the development of autoimmunity. The thymus is an organ of the lymphatic system where specialization of T cells, the regulators of the immune system, occurs. Thymus atrophy is one of the most significant risk factors for autoimmune disease development. A reduced thymus size results in a shortage of the cells that would otherwise target and destroy the immune cells that have "gone rogue" and targeted body tissue. If these rogue cells are not caught, they are unlikely ever to become "deactivated" since their target (i.e., you) is never entirely

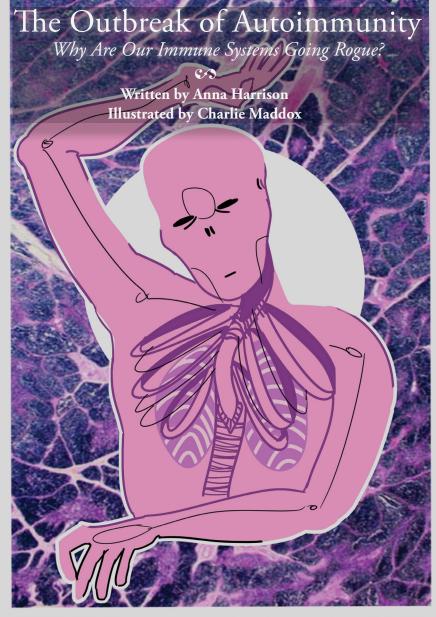
Autoimmune diseases represent a family of illnesses categorized by the body's immune-mediated attack on itself. The targeted organ, tissue, or cell characterizes type of autoimmune the disease; some of the most common include celiac disease, multiple sclerosis, autoimmune thyroiditis, and type-1 diabetes. Of the more than 90 different types of autoimmune diseases, scientists are currently funded to study less than half of them, and not a single one has a cure.

In the last three decades, the number of autoimmune disease diagnoses has more than doubled. Changes in environmental conditions such as chemical usage, medication, and diet are widely suspected to be the culprit of this outbreak.

We're going to investigate these three suspected factors, but before we delve into why things are going wrong, let's first understand how.

# How does autoimmunity begin?

The development of autoimmune disease is linked to genetic predisposition and continuous low-grade systemic inflammation. This inflammation is caused by psychological stress and



autogens, or particles that enter the body (topically, via inhalation, or via ingestion), which can activate the immune system.

One way particles enter the bloodstream is through the intestinal wall, which is becoming increasingly permeable in a rising number of individuals. The particles (from food or bacteria) that leak from the gut to the bloodstream are often identified as foreign by the immune system, which activates a targeted response against this substance. This is frequently the way dietary sensitivities and allergies begin and is linked to autoimmune disease development.

Damage to immunoregulatory mechanisms and glands, such as

chemical was found. A study of nine American's revealed an average of 91 industrial compounds, pollutants, and other chemicals present in their blood and urine [10]. In 2005, two major laboratories found 287 industrial chemicals and pollutants in the fetal cord blood of ten newborn infants. A 14-year study showed that farmers who worked with crops and were therefore exposed to more pesticides were more likely to die from an autoimmune disease or possess antineuronal antibodies (a known autoimmune marker). Another study showed that 100% of pregnant women carry pesticides in their placentas. So it's clear that these toxins have made their way into our bodies. But can these chemicals really cause

eliminated.

Now that we understand what goes wrong, let's investigate why.

### Novel Chemicals

During the mid 20th new chemicals century, were discovered, and massproduction and distribution of everyday "luxury" items containing novel chemicals became a hot market. By the 1940's, these chemical rich items permeated every American household. From pesticides used for crops to nonstick pans, non-flammable sheets, household cleaners, and pest-control, America became inescapably toxic.

While companies are required by law to test if their products are carcinogens (cancer-causing), they are not required to test if their products are autogens (inflammatory/autoimmune disease-causing). As a result, the vast majority of the chemicals present in almost everything we come in contact with are autogens.

There is growing evidence that the average modern American carries an abundance of chemicals and heavy metals in their system. In 2004, the CDC tested for 116 different chemicals in 2,500 individuals, and in every person they tested, every

#### autoimmunity?

While causation is difficult to prove, current evidence suggests the answer is yes. Even small doses of common chemicals disrupt the body's delicate endocrine system. The chemicals enter the bloodstream topically, through inhalation, or ingestion and occupy estrogen receptors. These estrogen "mimickers" cause unnatural biological responses; namely, the body receives the message that it no longer needs to make estrogen. Estradiol, in its natural biosynthesized form, plays a role in pathways of all primary innate and adaptive immune cells. Many hormones (especially sex hormones) are involved in immune regulation and the development of autoreactivity through their role in lymphocyte maturation, activation, and synthesis of antibodies and cytokines.

Studies show that sex hormones are indeed a factor in the pathogenesis of autoimmunity and that the expression of sex hormones is altered in people with autoimmunity. This correlation may explain why 80% of people diagnosed with autoimmune diseases are women. The common onset of autoimmune diseases during periods of hormonal fluctuation such as puberty, pregnancy, menopause, and emotional trauma supports evidence of this hormonal link.

Another study done in 2005 on female mice, which have a high predisposition to developing an autoimmune disease (like the known 25% of the human population with a high predisposition). Researchers exposed the mice to organochlorine pesticides (the most common type of pesticide found in everything from dairy and meat to breakfast cereals), and every single one rapidly developed lupus. The level of organochlorine pesticide that the mice were exposed to was four times lower than the level set as acceptable by the EPA .

Epidemiological cluster studies support this conclusion as well. For example, those who attended an elementary school in El Paso, Texas between 1948 and 1970 had double the expected rate of MS. This elementary school was located one mile east of a factory which processed a slew of heavy metals and emitted high levels of sulfuric acid. Several other studies have shown similar findings, including one in Buffalo, NY, where a toxic waste facility likely caused an unusually high rate of lupus.

#### **Antimicrobial World**

In many ways, the human body evolved to function differently from the way it functions now. Stress, for example, evolved as a momentary survival mechanism useful in high, acute doses, but is detrimental when present chronically. The immune system evolved to ward off pathogens. The hygiene hypothesis suggests that an increasingly sterile environment as a result of the advent of many antimicrobial drugs and compounds has left the immune system unprepared to face infections that their ancestors did, therefore leaving us more susceptible to allergic and immune disorders. Some migration studies support the hypothesis, such as incidences of subjects migrating from low-incidence to high-incidence countries who are more likely to acquire immune disorders.

When the amount of inflammatory toxins and chemicals being consumed by an average American is considered, it becomes increasingly clear that the issue isn't that we are not introducing things for the immune system to target, it's that we are introducing entirely different things than our ancestors did and in entirely different ways.

The environment became increasingly sterile since the invention and broad use of antibiotics in medicine and agriculture. This supports that we are not coming across microbes the way we used to and that our internal flora is altered as well, which is suspected to increase intestinal permeability and contribute to subsequent autoimmunity.

#### The American Diet

During the boom of mass manufacturing in the early 20th

century, highly processed foods became a household staple. The modern Western diet is characterized by over-consumption of refined sugars, salt, and saturated fat, as well as a reduced dietary variety. The inflammatory nature of these foods, as well as the toxins they contain (chemicals such as pesticides, herbicides, and antibiotics), can be detrimental to the human body. This leads to an altered microbiome (namely decreased microbe diversity), increased intestinal permeability, and continuous, low-grade inflammation, which all increase the likelihood of developing autoimmunity.

Over-consumption creates immune distress. Adipocytes (the cells specialized for storing fats) release proinflammatory markers including interleukin and tumor necrosis factor. A 2012 study showed that in animal models, these inflammatory markers act as false alarms that, over time, can cause the entire immune system to adjust to the high levels of inflammation, and become less responsive.

The food staples of the Western diet themselves are inflammatory. Simple sugar reduces white blood cell phagocytosis (immune cells engulfing and destroying infectious agents) and increases inflammatory cytokine markers in the blood. High amounts of salt induce inflammation and hold potential to worsen autoimmune conditions in animal studies. There is also ample evidence supporting the harmful immune-related effects of high levels of saturated fat. It feeds into several proinflammatory pathways and increases macrophage activation, altering the fatty acid membranes of immune cells, critical factors in antigen detection.

As the burning of fossil fuels increased, the atmosphere, ocean, and ultimately the fish supply became riddled with high levels of heavy metals such as mercury, gold, and silver, which can induce lymphocyte proliferation and subsequent autoimmunity.

#### Conclusion

We are living in a world that is both too dirty and too clean. The world is too clean because our society is fixated on creating an antimicrobial environment, and we don't encounter pathogens the way our ancestors used to. Our world is too dirty because we have saturated it with toxicity through immune activating and endocrine disrupting human-made chemicals.

Unlike 10,000 years ago, evolution will not likely "solve" this issue, and the epidemic will continue to spread unless we increase awareness, fund research, and critically examine consumer behavior.

Millions of people are developing autoimmune diseases. These chronic "mystery" diseases take, on average, 4.5 years to properly diagnose. In the future, it is expected that the exponential trend of autoimmune prevalence will continue: especially considering how once an autoimmune disease is developed, an individual is much more likely to develop another and pass it along to their offspring.

Seemingly trivial decisions have profound effects on our health and likely the health of generations to come. In modern society, individuals must question the safety of the products they consume. While the FDA goes through extensive testing to approve products, their process is based on what has been proved beyond any reasonable doubt. The amount of time it takes for environmental factors to induce an autoimmune disease is too long to be studied easily without proper funding.

All this being said, more scientific research is being focused on this area, more doctors are taking the crisis seriously, and some doctors are beginning to understand how to treat and prevent autoimmune diseases. This field of medicine moves toward proactive evaluations of genetic markers and individual environmental risk factors. However, the exact causes of developing autoimmune diseases are yet to be proven. Until that point, it's vital that citizens understand their risk and susceptibility of developing autoimmune diseases. েত Written by Nathalie Weiss Illustrated by Parker Shatkin

lthough it may sound shocking to suggest that hand dryers - devices that save trees by replacing paper towels - are harmful, these environmentally-friendly devices may actually be dirtying your freshly-cleaned hands. When someone flushes a toilet in a public bathroom, fecal bacteria can be thrown up to four and a half meters into the air. The hand dryers in the bathroom then suck the bacteria up out of the air and expel it onto your hands when you dry them. Researchers at the University of Connecticut's School of Medicine exposed petri dishes under a hand dryer for thirty seconds twelve inches from the nozzle and compared them to plates left out in the still air in the bathroom. The plates underneath the dryers had between eighteen and sixty colonies on average growing on them, with an extreme as high as 254 colonies, while the plates simply left out had less than one colony on average. And if this isn't enough to make you swear off hand dryers forever, knowing where these bacteria are coming from is even more disturbing.

Hand Dryers

Germ Machines in Disguise?

To uncover the origin of these pesky germs, researchers at the University of Connecticut and Quinnipiac University tested to see if the bacteria inside the hand dryers were multiplying inside the dryers themselves or if they were being pulled in from the air in the bathroom (fecal matter!) The researchers attached filters to the dryers to stop most of the bacteria in the air from being sucked into them. When more Petri dishes were put under the dryer after this had been done, there were 75% fewer bacteria on the dishes. The researchers explained that one reason that hand dryers dispense so much bacteria is that there is a lot of air passing through the dryers — 19,000 linear feet per minute at the nozzle. The convection that the high airflow causes could also draw in the air from the room. Disturbingly, this means that most of the bacteria being blown out of the hand dryers originate from the bathroom air that is sucked into the dryers.

Unfortunately, traditional hand dryers aren't the only culprits guilty of covering your freshly-cleansed hands in bacteria. Jet air dryers the ones shaped like a "U" — seem safer because they don't have chambers. This suggests that bacteria are less likely to be sprayed all over your hands when you use these dryers because they don't have reservoirs for bacteria to grow in. However, these futuristic appliances are just as germ-infested as their outdated counterparts. A study carried out by researchers from Campden BRI in the Journal of Applied Microbiology compared the spread of viruses between traditional hand dryers, paper towels, and jet dryers. The researchers collected this data by dipping their sterile, gloved hands into a harmless virus called MS2. They then shook off their hands and dried them either under a traditional hand dryer or a jet dryer or with paper towels. A blast of air going 430 mph comes out of the jet dryer when it's in use. This dryer spread the viruses much further than the two other methods,

nine feet; the traditional dryer spread them less than three feet. The moral of this study is that all dryers are germy, period, but some are germier than others.

Hand dryers make a great home for bacteria because the warm air combined with the moisture of a bathroom is a perfect environment for growth. A study carried out at the University of Westminster found that using hand dryers actually increases the presence of germs in a room by 225%. Although a lot of us may feel a pang of guilt when using paper towels because of their impact on the environment, they are a much safer option to dry

your hands with because they do not spread germs from others who have used the bathroom before you. Studies show that they are able to help prevent contamination from residual bacteria and are a healthier option for us as humans, although not for our planet.

Even though paper towels will most likely never be as environmentally-friendly as hand dryers, there is a potential way to decrease the negative ramifications. The creation of 100%-recycled, compostable paper towels has opened up new opportunities to be ecosensitive while still avoiding hand dryers. One company, called If You

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Care, has created a unique brand of compostable paper towels. Their paper towels are made from a blend of cellulose, non-GMO unbleached cotton, and mirabilite (a mineral salt.) During production the minerabilite is washed out, leaving behind a material made of 70% cellulose and 30% cotton, which is very porous. The paper towels can absorb up to sixteen times their own weight in water and do not leave fibers on the surface of items. Best of all, these towels are reusable for at least one week and are tear-resistant. Although not quite as eco-friendly, compostable paper towels are great candidates to claim the places of hand dryers in public restrooms in the name of human health.

If you'd like to learn more about the germs spread by hand dryers, check out Alexandra Ossola's article "Do Jet Hand Dryers Really Spread More Germs Than Paper Towels?" published by Popular Science on April 14th, 2016.