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The Complexities of Curing a Disease

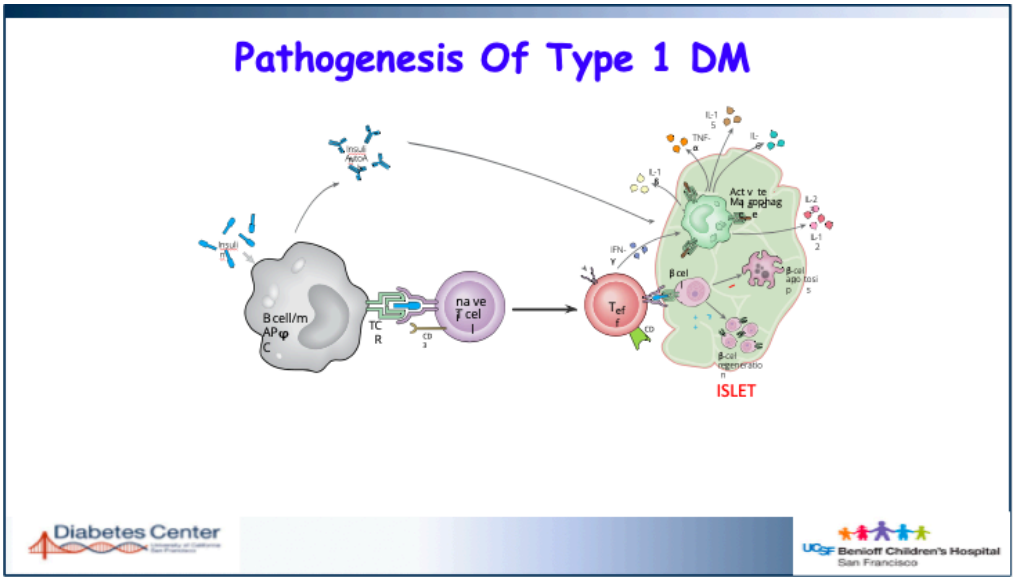
Abstract:

Ever since Type 1 Diabetes was discovered in 1899 by Joseph Merling, who removed dogs' pancreases and noticed the sugar levels in the dogs' urine spike, the need for a cure only grew in importance. Unfortunately, Type 1 Diabetes is not a simple disease with just one problem to eliminate. This paper will explain the complexities of curing a disease, the research, and the technology that makes life easier for Type 1 Diabetics until researchers can find a cure. The paper will present and discuss findings over the last decade of research that have made an impact towards a cure, as well as some people who have made a significant impact on Type 1 Diabetes research. It will introduce some organizations that help individuals with Type 1 Diabetes live better lives and have more stable management of blood glucose through access to insulin and other supplies throughout their daily lives. This paper will respond to questions similar to Have clinical trials helped the understanding of the disease and its possible cures? How has Type 1 Diabetes baffled researchers by its complexities of possible solutions that evidently end up with consequences? Finally, it will address the question; is funding important for the creation of clinical trials and drugs and how does money affect the way research is conducted?

Intro:

According to JDRF, more than 37.3 million Americans suffer from Type 1 or Type 2 Diabetes every day. In the last year alone, 64,000 people in America were diagnosed with Type 1 alone. Type 1 Diabetes diagnoses have been on the rise in the last decade and the trend line is still rising. Yet, so many people have never heard of the disease.

Type 1 Diabetes is brought on by an autoimmune reaction that causes the body's white blood cells to attack the insulin-producing beta cells.



Slide created by the Diabetes Center at UCSF Benioff Children's Hospital

Without insulin, the body cannot turn carbohydrates, fats, and proteins into energy, and the excess sugars start to flow through the bloodstream causing high blood glucose. Before diagnosis, many pre-diabetics will lose weight, have low energy, frequently urinate in an attempt to rid the body of the excess sugar, and drink lots of fluids due to frequent urination. If left alone for too long, a person with diabetes can develop Diabetic Hyperosmolar Syndrome, which is a scientific term for a diabetic's blood to be thick and syrupy caused by the excess sugar. If still

left untreated, diabetics can go into a coma resulting in permanent brain damage or death. More than 85,000 people die from diabetes annually.

Purpose for paper:

Diabetes is not a simple disease. Many factors come into play when developing a cure, and there are often more setbacks than steps forward. This paper will examine why diabetes has not been cured yet, all the steps that have been taken to get to where we are now, and the ways researchers are currently looking to cure this disease. This paper can help support newly diagnosed patients and parents of those patients to understand the current research being done and better understand the process of curing any disease in general.

When summarizing findings, varied sources were utilized to look at different research being done in various aspects related to diabetes. Currently, researchers are looking towards a cure by using a drug that already exists to serve the purpose of helping a diabetic. One example of this was a phase three clinical trial run by the University of Florida's Diabetes Institute as well as other locations that focused on combining two drugs in the hope that the researchers could extend the time beta cells produced insulin during the onset of Type 1 Diabetes. These drugs were called ATG or Antithymocyte globulin and G-CSF or Granulocyte-colony stimulating factor. ATG was originally created to help treat or prevent acute cellular rejection after organ transplantations and was also used as a therapy for people with acute aplastic anemia. G-CSF was created to stimulate a patient's bone marrow to produce granulocytes and stem cells and release them into the bloodstream. It is also used in cancer patients undergoing chemotherapy. The study was split into three groups. The first group would take ATG, the second would take both ATG and G-CSF, and the third group would take a placebo. At the end of the study, it was found that the group that took only ATG had the most longevity in insulin-producing beta cells.

ATG is also available through certain endocrinologists for newly diagnosed children who meet specific criteria. This research and other research that has been done is very important to finding the possibility of a cure. It could also provide general information for other researchers about what successes and setbacks happened and what could be researched further. All the information that one team of scientists produces can be considered by another team across the globe and be used differently. There is a possibility that one team who looks at it will see something different from the original team.

The general conclusion that will be drawn by the end of the paper is that curing a disease is no easy task and requires thousands of minds working towards a solution. Type 1 Diabetes is a very complex disease that requires a wide variety of research in order to have even a basic understanding of the ability to find a cure.

The research for this paper was acquired from a visit to the University of Florida's Diabetes Research Institute to learn about the aspects of research being conducted on the disease. Additional information was supported by websites, books, and slide presentations created by experts at the University of California San Francisco, and the University of Florida's Diabetes Institute. The guiding questions to drive the research were: Why is Type 1 Diabetes so hard to cure? What research has been done to start the development of a cure?

These questions cover the topic of the paper as well as interest to the author. One important thing quickly realized was how much researchers worldwide are doing for the cause. Many people, such as Dr. Mike Haller at the UF Diabetes Institute or Dr. Stephan Gitelman at UCSF, lead research studies such as the ATG/G-CSF as well as scientific speeches all over the world that can help inform people on the current state of research and inspire others by showing them how far we have come to contribute to the cause. Many of these researchers also run or

help operate organizations that strive to create a better world for people living with Type 1 Diabetes by helping to supply them with Insulin, insulin pumps, continuous glucose monitors, and finger blood glucose testers, especially in countries where this technology may not be widely available. Overall, there are millions of people on a global scale who are putting their all into creating a better world for people with Type 1 as well as people who may develop it during their lifetime.

Many people ask, how on earth did the covid vaccine come out so fast when Type 1 Diabetes has been without a cure for decades? The difference between the Covid vaccine and Type 1 Diabetes is that Covid is a global emergency, and corners get cut. Researchers started working on the Covid-19 vaccine in January 2020, immediately after the vaccine became a global problem. Due to the urgent nature of Covid-19, researchers were able to use special access funding to get all the money they needed to create a vaccine. The finding also helped researchers get through the clinical trial phases quickly. The phases included Phase I (testing safety/side effects on a very small group of people) and Phase II (testing how well the drug actually works). These were done in about six months instead of the typical two years and this enabled researchers to move onto Phase III trials which are mostly final tuning for dosage. Once considered safe, the drug was immediately mass-produced before knowing the results of Phase III trials in order to save time. The reason for this being the death rate for covid was only increasing and the researchers knew that it would work at least a little.

Unfortunately, this emergency funding is not the case when researching vaccines, cures, and treatments for Type 1 Diabetes. One of the biggest issues researchers face is that they do not understand how one develops Type 1 Diabetes. Most say it is the white blood cells gone rogue, while others may suggest the insulin-producing beta cells mutated or got inflamed and that

caused the attack. Either way, it is hard to develop a cure for something so widely complex. This is the explicit reason funding for this research is so important. With so many angles to look at Type 1 Diabetes, research money is being split into hundreds of areas to help cover all the possible theories and tests that researchers think could impact the curing process. The best possible solution researchers could create is a biological cure that lets a diabetic's body start producing insulin again without any repercussions or immunosuppressants needed. This would be the easiest solution if we knew how one developed diabetes. Another way researchers could look at a cure for Type 1 Diabetes is through a vaccine. The difference between a vaccine and a cure for Type 1 Diabetes, is that a vaccine stops the onset of the disease-preventing beta-cell destruction and lets a person live life without risk.

In contrast, a cure would reverse the effects for someone who already has Type 1 Diabetes. Vaccines are a great way to prevent any new number of diseases from arising, but they would not have any effect on someone who already has the disease. Another important aspect to look at when curing a disease is clinical trials and approval from the Food and Drug Administration or FDA. The two most important things researchers look at when considering a drug is whether it works and whether it is safe. These two precautions are also looked at when the FDA chooses drugs to go into testing. "Clinical trials are one of the most important steps in a cure creation process," says Hannah Nichols, an author for Medical News Today. Phase I, II, and III trials allow researchers to test and tweak drugs to discover proper dosing, how well the drug works and how much should be given to serve the purpose but not have any serious side effects. Clinical trials are the longest process after a drug is created and that is because the process is very complex. With words said by the National Institute of Health, "Clinical research is medical research that involves people like you. When you volunteer to take part in clinical research, you

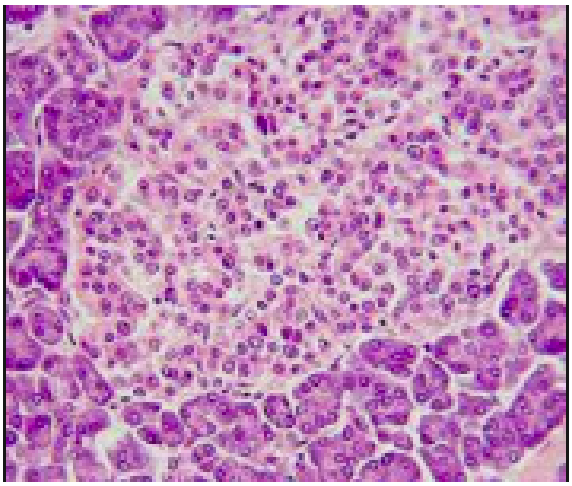
help doctors and researchers learn more about disease and improve health care for people in the future. Clinical research includes all research that involves people." Bringing in diverse groups of people for these trials helps researchers test on many different variables. Not every human volunteering to be part of a trial is exactly alike. Some might have certain conditions, others might have certain allergies. Due to the random nature of the test subjects, this allows researchers to consider thousands of possible side effects that could occur and can allow them to decide if the drug is worth moving forward or if it needs to be recalled and worked on more.

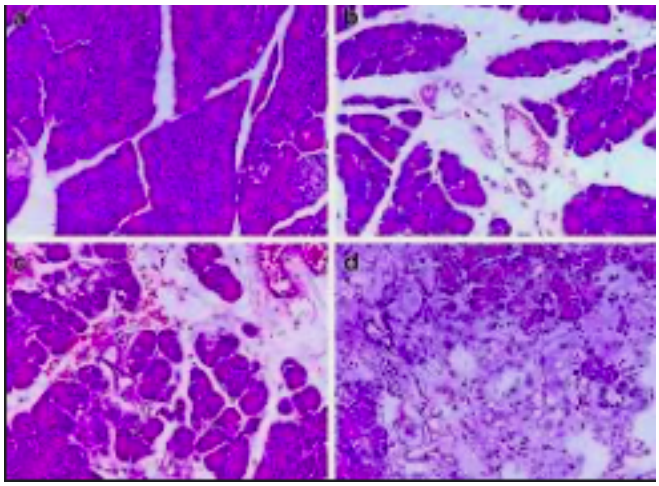
The next important part of clinical trials come down to the FDA. The Food and Drug Administration is in charge of deciding if each and every clinical trial for Type 1 Diabetes and every single other disease out there is allowed to happen. The FDA will look at the data the researchers have done to determine if the trial would be safe, serve a purpose, and work exactly as the designers intended. In an interview conducted as research for this paper, Dr. Haller, the Chief of Pediatric Endocrinology at the University of Florida said, "There is nothing the FDA cares about more than the life of a child". This brings us to the subject of pediatric trials versus adult trials. Clinicaltrials.gov is the main source of clinical trial action. If somebody wants to participate in a trial, this is the first place to start looking. When looking at clinical trials for Type 1 Diabetics between the age of birth and 17, there are studies such as, Supporting Parents of Young Children With Type 1 Diabetes in Closed-Loop System" and "Insul-In This Together Program for Adolescents With Type 1 Diabetes and Their Parents (IITT)" All zero risk studies that are aimed at supporting children and parents rather than testing new drugs. Then one can put in their age as and adult, they will start to get studies such as, "Monocyte Function and Inflammation in Type 1 Diabetes and Its Modulation" or "Prevention of Autoimmune Destruction and Rejection of Human Pancreatic Islets Following Transplantation for Insulin

Dependent DiabetesMellitus" There are some trials aimed for children that are more intense. Through personal experience, one trial was targeted at children testing Medtronics first closed-loop system. A closed-loop system is an insulin pump that works in combination with a continuous glucose monitor to suspend insulin delivery when the body's blood sugar is low, and increasing insulin delivery when the blood sugar is high. This trial required participants to stay overnight in a hospital with two IVs in their arms getting their blood sugar checked every 15 minutes to test if the insulin pump would work. This was a very long night for all the participants and left them feeling minorly anemic to the amount of blood that had been taken from them in the last 12 hours and from being so sedentary. This trial was extremely beneficial to the understanding of closed loop technology and spurred many other companies to start researching their own closed loop systems as well. Overall, 90% of trials aimed at children will have a severely lower risk than adult trials because of the ethics of putting children through these harsh conditions.

One specific field of research that is interesting is the research Mollie Huber is conducting on nPOD samples at the University of Florida. An nPOD or "Network for Pancreatic Organ Donors with Diabetes", sample is a pancreas that has been ordered by researchers. There is a massive data bank that has information on thousands of donors' pancreases. Huber can choose what she is looking for in a pancreas, the age of the person who had the pancreas, and even the gender of the person the pancreas was from. nPOD samples are incredibly important to Type 1 diabetes research because they allow researchers to examine pancreases with or without Type 1 Diabetes. Huber can look for differences between the two, do cell tissue samples and stain the cells in the pancreas to get a real look at what is happening in a diabetics pancreas. Cell staining is a technique that can be used to see cells and cell components under a microscope. By

using different stains, one can preferentially stain certain cell components, such as a nucleus or a cell wall, or the entire cell. Huber will stain cells in order to enhance visualization of the cell or certain cellular components under a microscope. Cells may also be stained to highlight metabolic processes or to differentiate between live and dead cells in a sample. This can be beneficial to





Type 1 Diabetes research because researchers can study how fast white blood cells kill the beta cells, or how fast a non-diabetic's pancreas produces insulin. The images above are what a pancreas looks like when stained for visual knowledge.

The most researched idea for a cure is developing a new drug or a new combination of two drugs. This process involves taking a drug that already exists, tweaking it, and using it to see if it affects a person with diabetes. The ATG/G-CSF is a perfect example of this. Researchers will reach out to companies with theories that suggest that their drug may work in another way. The companies will typically receive the drug for free because the pharmaceutical companies are more than happy with the possibility to market a drug another way and make more money. The National Library of Medicine says that, "Drug combinations of two or more compounds with different mechanisms of action are an alternative approach to increase the success rate of drug repositioning." The only problem with this process is that there are often issues with side effects

of taking a drug meant for another reason beyond Type 1 Diabetes. There are often many cases of serum sickness involved with these and as it varies from human to human, some side effects could be significantly worse than others. Serum sickness is the term used when a patient gets sick from the side effects of a drug or treatment. Serum sickness is also extremely helpful to researchers because if many people have the same serum sickness, they can adjust the drug dosage or the drug itself in order to create the best possible medicine.

In conclusion, the lack of a cohesive understanding of Type 1 Diabetes is what makes it so difficult to cure. From understanding exactly what Type 1 Diabetes is to getting funding for a specific type of research, and getting that research past the FDA, diabetic researchers certainly have their hands full. There are often hundreds more failures in the lab than successes, and every success only sets us half a step ahead. This can be the case for other diseases beyond Type 1 Diabetes. The biggest takeaway found through research and personal experience is that it is very hard to cure a disease if people do not know what causes it in the first place. Although the research being done for Type 1 Diabetes well surpasses a billion dollars, it is absurd to see just how difficult and open-ended this search for a cure is.

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