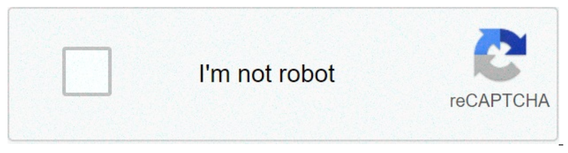

Continue

Non experimental research types

In the depths of the Depression, railroading lifted travelers' spirits with a bevy of pocket streamliners-fast, flashy, undersized, articulated trainsets like Burlington's Zephyr and Union Pacific's Streamliner.Twenty years later, in the mid-1950s, another flurry of futuristic, high-speed, undersized, articulated trains arrived on the scene. These came and went without significant impact, victims of unreliability and cramped accommodations."Train-X" had been unveiled as far back as the Chicago Railroad Fair in 1948, where-at the behest of gadfly Robert Young-a full-sized model of a coach had been displayed by Chesapeake & Ohio. By 1956, when the first Train-X (built by Pullman-Standard, with a locomotive by Baldwin) was delivered, Young was at New York Central, so the train went there too. New Haven's Patrick McGinnis, a Young crony, also bought a set.In addition, McGinnis ordered a "Talgo," one of three trainsets for U. S. railroads built by American Car & Foundry in cooperation with Patentes Talgo S.A. of Spain. ACF built a Talgo demonstator in 1949, plus trainsets that went to Spain to launch a fleet very much alive today.The third of the 1950s experimentals was the General Motors "Aerotrain," two train-sets of modified GM bus bodies powered by automotive-looking EMD diesel locomotives. After a year or so of touring and testing-with long-term stints on the Pennsylvania, New York Central, and Union Pacific-the Aerotrains were sold to the Rock Island, where they ran for some eight years in suburban service before being given to museums.Read more about the history of railroads with these articles:Railroad TestsMoffat TunnelRailroads of the 1990sRailroad Songs By Sara Tiner COVID-19 can affect people in a number of ways. Some can be infected and have no symptoms — what's known as being asymptomatic. Others have symptoms, but do not have a serious illness. And some can require hospitalization for intensive complications. For those with symptoms or those who are progressing to hospitalization, researchers are looking at what might work, and finding glimmers of hope in experimental therapeutics, both new and old. In the hospital, there are a few ways patients can be supported through this illness. There are two main categories of experimental therapeutics: antiviral drugs and immune modulators. Antiviral Drugs This group of drugs prevents a virus from copying itself. RNA interruption works because unlike human cells and DNA, SARS-CoV-2 carries its instructions for replication on RNA. Because viruses can't replicate on their own — that is, they are not alive in the same sense that people are — a virus must make more viruses by hijacking a host cell. Typically, antiviral drugs target one aspect of that hijacking/replication process and block it. The virus that causes COVID-19 is called SARS-CoV-2. It is in a family called coronavirus, so named for the way its spike, or S, protein appears under the microscope. That spike protein, along with other proteins — M and E — are embedded in a protective, fatty coating called a lipid envelope. It keeps the viral RNA, which is in turn protected in a nucleocapsid, protected until the RNA can be injected into a host cell. One example of an antiviral drug is remdesivir. Remedsivir blocks the translation of RNA that allows the virus to copy itself. According to data published May 22, 2020, in The New England Journal of Medicine, the drug shortened recovery time by four days among hospitalized patients, compared to a placebo. It was authorized by the FDA for experimental use to treat severe COVID-19 on May 1, 2020. Another experimental therapy being investigated for patients switches focus from the virus to the body's immune system. These drugs and therapies are based on drugs that exist for other purposes, as well as new drugs that are in development specifically for treatment of COVID-19. Immune System-Focused Experimental Treatment Called immunomodulatory therapy, these drugs focus on the response of the immune system to the virus. One group of drugs, called steroids, calms the immune system. People generally take a steroid for conditions such as arthritis, asthma, or as part of treatment for some cancers or flare-ups of multiple sclerosis. Steroids act on genetic instructions that kick off inflammation and the ways in which inflammation develops and keeps escalating. Researchers are determining if this type of intervention is helpful for serious cases of COVID-19. In one paper, published July 17, 2020, in NEJM a steroid called dexamethasone was reported to decrease the death rate, as measured at 28 days, of patients on ventilation or receiving oxygen from 41.4% to 29.3% and from 26.2% to 23.3%, respectively. SARS-CoV-2 (teal dots) on the surface of a cultured Vero cell (nucleus at bottom left). Image courtesy of the Mayo Clinic Microscopy and Cell Analysis Core Other immune modulating drugs focus on a part of the immune system called antibodies. These Y-shaped snippets of protein have various functions, but basically they attach to something the body needs to pay attention to and flag it for immune system attention. Here's an example: When a virus invades a cell, it drills through the cell's membrane, takes over and makes copies until the cell bursts, sending the new virus particles out to infect other cells. As the virus travels, some of these bad actors trip an immune system "red alert." After a series of events, immune cells called B cells transform into plasma cells and begin to churn out antibodies. Some antibodies are generalists and smother the invading virus, basically gluing it into an immobile, sticky mess. Other antibodies fit like a key into a lock on the virus membrane, blocking it from drilling into a new cell and continuing the process of replication. Antibodies are Y-shaped snippets of protein that attach to something the body needs to pay attention to and flag it for immune system attention. In the case of a virus, some antibodies smother the invading virus. Other antibodies fit like a key into a lock on the virus membrane, blocking it from drilling into a new cell and continuing the process of replication. According to an article in Nature, antibodies were first discovered in the blood of animals exposed to diphtheria or tetanus toxin more than 100 years ago. But it was difficult to isolate just one type of antibody and reproduce it for study. In 1975, researchers found a way to produce only the antibody they wanted by combining the cell producing that antibody with a myeloma cancer cell, which replicates without the normal cellular breaks on division. The cells were cloned and grown until a line was isolated that produced only the target antibody. Eventually, they were called monoclonal antibodies. Drugs based on monoclonal antibodies are designed to push the immune system into action or block its activity. These drugs can also help researchers develop new ways to diagnose and treat disease. These drugs tweak, or modulate, specific antibodies. COVID-19 and Monoclonal Antibodies In terms of COVID-19, monoclonal antibodies are being examined as a treatment for patients with severe disease and a way to boost immune response (called passive immunity) among people for whom a vaccine is not effective or recommended. Researchers are examining the antibodies from recovered patients to identify which are most effective at blocking the virus from hijacking cells, or managing the immune response SARS-CoV-2. The vast majority, to date, target the SARS-CoV-2 spike protein that helps the virus infect a human cell. Hundreds of companies in dozens of countries are researching antibody-based therapies to treat COVID-19 or prevent it in people who are at high risk for severe disease. In the meantime, researchers are also combing through existing monoclonal antibody drugs to determine which ones might be helpful in treating COVID-19. ClinicalTrials.gov lists about a dozen studies using monoclonal antibodies, alone or in combination, in the context of COVID-19 infection, pneumonia, lung injury or acute respiratory distress syndrome. The candidates are on the market to treat diseases as common as cancer or rheumatoid arthritis, or as rare as hemophagocytic lymphohistiocytosis. One example is the drug lenzilumab. It blocks an immune chemical "red alert" that leads to a call for more white blood cells, such as monocytes, macrophages and granulocytes. The drug is approved for treatment of asthma, rheumatoid arthritis and leukemia. Trials are underway to determine if this monoclonal antibody can moderate damage caused by the immune system during a severe COVID-19 illness. Separating the Wheat from the Chaff Some data are already known about monoclonal antibody drugs. Two of the first studied drugs, sarilumab and tocilizumab, both focus on a chemical used by the immune system to communicate called interleukin 6. Released by white blood cells during infection, interleukin 6 ramps up immune actions and inflammation. But if the tight control of interleukin 6 fails, the result can be unceasing inflammation and eventually an autoimmune disorder. The monoclonal antibody drugs block the receptor for interleukin 6, thereby preventing it from from reaching cells. However, both drugs failed to show benefit against placebo or standard treatment of COVID-19 patients. But IL-6 is only one target. Researchers around the world are taking apart the SARS-CoV-2 virus and uncovering how the immune system responds to this new human virus. According to the Antibody Therapeutics Tracker, at least 243 companies in 26 countries are pursuing antibody-based therapies for 48 targets on the virus or in the immune system. From discovery labs to the final stages of drug approval, researchers worldwide are hoping to assemble a toolbox of new monoclonal antibodies to manage COVID-19. Convalescent PlasmaThe most historical option for moderating the immune system is to use the antibodies created by people who've already recovered. These antibodies are collected from the blood of former patients and given to patients with severe COVID-19 disease. On April 1, 2020, Mayo Clinic was selected by the FDA to start an "expanded access program" for COVID-19 convalescent plasma administration to patients. The nationwide program published data on the therapy's safety and possible signs of how it might help patients. Based on those reports, convalescent plasma met the standard for FDA's Emergency Use Authorization, and the expanded access program was discontinued. The authorization means patients can continue to receive convalescent plasma while research at Mayo and across the world continues. Medical Illustration of normal cells (pink) and senescent cells (green). Credit: Donna DeSmet, Mayo Clinic medical illustration/animation From the Old to the New From historical wisdom to one of the newest ideas in aging research, COVID-19 researchers are leaving nothing that might work out of the mix. Mayo Clinic researchers are investigating a new type of drug called a senolytic for supportive treatment for COVID-19 patients. Senolytic drugs target what's known as senescent cells. These are cells that the body has directed to shut down but that refuse to die. Senescent cells, or zombie cells, have been linked to numerous diseases of aging but now a drug that targets these cells is under investigation for COVID-19 treatment. In one clinical trial at Mayo, researchers are examining if the drug can prevent COVID-19 patients from getting worse, as measured by the need for increased breathing support, general measures of frailty, or by progression from mild COVID-19 to severe disease. By aggregating large numbers of patients in these efforts, starting clinical trials like the ones underway at Mayo, and collecting data in programs like the convalescent plasma effort, researchers will over time be able to separate what works from what does not, and what may be harmful. Learn more Read more stories about advances in individualized medicine. Register to get weekly updates from the Mayo Clinic Center for Individualized Medicine blog. Join the conversation For more information on the Mayo Clinic Center for Individualized Medicine, visit Facebook, LinkedIn or Twitter at @MayoClinicCIM Tags: covid-19, individualized medicine, Uncategorized Recently, Adobe shipped me a copy of their Master Suite CS4, which I use for benchmarking CPUs (and maybe GPUs, too, in the future). I've been using After Effects for benchmarking for several years now, and just started using Photoshop for performance testing.So naturally, I loaded it up on my production system and started a video project, using Premiere Pro CS4. Since this was a downloaded version Adobe had supplied, I didn't have a manual.Now, I'd never used any version of Premiere in the past, although I have used consumer grade video editors once or twice, like Avid's Pinnacle Pro 11. A professional level application like Premiere Pro can be intimidating. They're typically tremendously flexible, which is their strength, but the learning curve can be pretty steep.Within a few hours, I was able to drop in clips, figure out how to trim, edit and apply effects, as well as do basic titles. Adobe's online help system was completely useless to me. I could either watch video tutorials (lame) or search their support site to get a bunch of vague references to what I needed that had no pertinent information. Whatever happened to installing local help files that replicated what was in the manuals?Despite this lack, I was up and running in Premiere Pro CS4 in fairly short order. It probably helped that I'm a fairly experienced Photoshop CS3/CS4 user, but only a little, since the user interfaces and jargon are notably different.A couple of days ago, my wife started using a new phone. Bear with me, this is not a change of subject.Actually, she started using my old HTC710, which is Windows Mobile based and a big step up from her old, basic Nokia. I walked her through the steps of turning it on, using the built-in QWERTY keypad and making calls. Later on, I'll walk her through the process of syncing Windows Mobile to Outlook on her laptop.Now, my wife is a fast learner, but she wants to be taught. She also learns very well from documentation. Whenever she acquires a new piece of hardware or software, she spends a large amount of time reading the manual. Afterwards, she generally understands it all quite well. (The only exception to this has been the HDTV system, but a Harmony One universal remote cured that.)My two daughters also learn differently. Emily, my younger daughter, likes to read manuals. When she gets a new board game, for example, she reads the rules, cover to cover. When we play, she knows the rules back and forth; in fact, she knows them so well, she's become the classic "rules lawyer," able to exploit loopholes at will.My other daughter, Elizabeth, will dive in and try to do stuff. Sometimes that results in a cry for help, but mostly, she figures stuff out pretty well, heading to the manual only to find out how to do something very specific.People do learn differently. In my career as a writer and manager, I've noticed what seems to be two fundamentally different learning styles. I call them the Experimenter and the Student, for convenience. Neither style is better than the other, in general, but there may be specific instances where one style may prevail. The Student, who wants to learn from a teacher or from documentation, may take longer to come up to speed—but in the end, may have a more thorough grasp of the topic at hand.The Experimenter can get up to speed very quickly. But depth of knowledge can take longer and often has holes in knowledge for a long time. They also tend to rely on techniques learned, even though more efficient methods may exist, but require some external learning (like a teacher or good manual).Experimenting can also be expensive, as I've learned the hard way. I've killed hardware by fooling around with it, when a quick trip to the manual would have saved my bacon.I definitely fall into the Experimenter category. Most of my knowledge about PC technology has been self-taught, though having a physical science background helps. My wife is most definitely a Student. Elizabeth is probably a blend of the two, willing to dive in and figure stuff out, but there are times when she really wants a good teacher.What type of learner are you? Do you love soaking up information from a good teacher, or do you just prefer to dive in and figure it out? Dive into our forums and let us know.