Viruses, Vaccines, Mutations, Evolution of Influenza

From http://www.college.ucla.edu/webproject/micro12/m12webnotes/viralevolution.htm

Since viruses have such high mutation and reproductive rates, they can adapt to changing environments quite well. Indeed, since the only way they can reproduce is by infecting a cell they must be able to evolve faster the their hosts cells. If not, then the host cells would adapt/evolve to where a virus would no longer be able to infect. Cells change their surface receptors so viruses cannot attach; the viruses change their surface proteins so they can attach to the changed cell surface receptors. The viruses must always stay ahead of the evolution game. They are very, very good at this.

Viruses must always have their host around to reproduce. If the host becomes extinct then the hosts' viruses become extinct as well. So, it is advantageous for a virus to "cross-over" into a new host every now and then. We will cover this in a few more lectures. Another problem some viruses have is that they must have "fresh" hosts to infect. Since animals have fairly well developed immune systems that can remember and prevent subsequent infections, viruses need to get around this problem. If every animal has immunity then the virus is stranded and will not be able to reproduce. These viruses must have a steady supply of new victims. This means there must be critical minimum population density to maintain some viral infections. These types of infections are sometimes called "crowd or herd diseases". We will go over the history of these viruses in a few more lectures but for now lets take a look at how a couple of these have been eleminated (or close) in the human population.

Let’s take the diseases smallpox and polio. These viruses only infect humans, have no intermediary hosts, and they cannot survive for very long in the environment. If a person is infected and survives, they will have life-long immunity. So the viruses must always have fresh hosts to infect. In the past there has always been a steady supply of new victims (Children, step right up!).

With the discovery of vaccines it is possible to provide everyone with immunity before they get sick. This is what has happened with smallpox. Through a worldwide effort of vaccination and containment, the last naturally occurring case of smallpox was in Somalia in 1977 and it was declared eradicated by the World Heath Organization two years later in 1979. Polio was the next target. It was hoped that this would be eradicated by 2000, but the project is a little behind schedule. Maybe by 2002 or 03 it will follow smallpox out of the human population. Diseases that killed, maimed, and disfigured millions no longer exist!

These viruses are DNA viruses and always relied on a minimum population density to provide new hosts to infect. Their environment was steady and they did not have to evolve or adapt very fast in order to reproduce. When we intervened with vaccinations they could not evolve fast enough to overcome our immune protection (our immune memory). Nobody pities the poor little viruses! May they R.I.P. Smallpox might not, but more on that later.

The University of North Carolina has done tests and found that viral mutations occurred. [More often when selenium was lacking. Vaughan Jones.]

Some viruses solve the host numbers problem by overcoming the animal's immune memory by changing or mutating into a slightly different virus that can infect the same host over and over. If a virus has a high mutation rate it can overcome our immune memory by changing its surface proteins, so the antibodies that are produced no longer attach. The RNA viruses are good at this. HIV that causes AIDS mutates so fast that the immune system never clears it from the body and every vaccine that has been developed has failed to prevent infection from this ever-mutating virus. After time the vaccines fail because the virus changes its' surface proteins where any antibodies produced no longer recognize the virus. It is like a "new" virus. With HIV this unfortunately results in a life-shortening infection. The RNA retroviuses like HIV have the highest mutation rates ever measured.

The RNA viruses that do not go into latency (not retroviruses) have lower mutation rates (but higher than DNA viruses). A good example is the influenza virus. Every year there is a flu season in the Fall and Winter months. The influenza virus has two main surface proteins that allow the virus to infect. These are the "H" and "N" proteins. When we are infected (or vaccinated) with flu we develop memory antibodies against the "H" & "N" proteins. Thus, they are sometimes called the "H" & "N" antigens (Ag's). The antibodies produced will prevent subsequent infection if we are exposed to the same flu virus. However,

as the flu virus travels around the world following the local flu season, it mutates. If the RNA that codes for either the "H" or "N" Ag mutates then the protein will be slightly different and those antibodies will no longer bind. Now, the chances of having both the "H" and "N" antigens mutate in a given year is really small. So, chances are that only one of them will change. When this happens and we are exposed to this mutated virus during next years flu season some of our antibodies will bind and some will not. Those that bind to the non-mutated protein will still give us some protection. Those antibodies against the mutated protein will no longer work. So, the infection will be mild but infect a lot of people. This process of gradual mutation from year to year is called antigenic drift and leads to yearly epidemics of flu. Every year the CDC determines how the flu virus has mutated and makes a new vaccine based on these new strains. So, every year we get a new flu shot.

The flu virus has another way of overcoming our immune system. It can rearrange its RNA by mixing with other flu viruses to create hybrid viruses that have new "H" & "N" antigens in the same virus. These viruses are like completely "new" flu viruses because nobody has any antibody memory against them. They are particularly nasty and can infect a lot of people fast. These viruses cause pandemics of influenza. This only happens when the flu virus from two different species infect the same cell. Flu viruses tend to be species-specific. There are human, horse, pig, chicken, and duck flu viruses. Ordinarily they will not cross-infect. But, if a human is in close contact with one of these animals when the animal has their flu, sometimes the virus can infect the human lung. This is usually a very mild infection and is not spread to other humans. But if this human also has a human flu virus infection at the same time then the two viruses can be found replicating in the same cells at the same time. This is not good! The viruses that come out of this cell have their RNA molecules rearranged and some of them might be mostly human influenza but with animal flu "H" & "N" Ag's on their surface. This is a big change, or antigenic shift in the virus. The chances of this happening is very remote. However, over time it does happen (about every 16 years).

So, the CDC monitors flu around the world looking for antigenic drift and shift. If a drift is detected they anticipate a nasty flu season and recommend the very young, very old, and people with weakened immune systems to be vaccinated. If a shift is detected they use drastic measures to prevent a pandemic. In 1976 they detected a shift from pigs into pig farmers. President Ford recommended that everyone in the United States be vaccinated against this swine flu. The pandemic never occurred. Was it due to a false alarm or did the massive vaccination campaign prevent rapid spread? We will never know for sure. More recently, in 1997, several young people in Hong Kong died of flu. it was determined that a shift crossover had occurred in the chickens. Every chicken in Hong Kong and southern China was killed to prevent the infection from becoming established in the human population. Again, no pandemic occurred. False alarm or effective defense? It is probably better to be safe than sorry.

One of the worst pandemics of flu occurred in 1918. This has been called the Great Pandemic. It killed 20~40 million people worldwide including 500,000 in USA alone. It was one of the major factors in the end of W.W.I. More soldiers died of influenza in the Fall of 1918 that by bullets in the entire war (Hmmm.... biological weapons....). Not much was known about how flu operates back then so nobody knows what exactly happened, but most of the people that died were young and healthy, not the usual elderly victims. So, it was probably a major genetic shift. Scientists are still trying to figure out what happened. They are looking for fresh frozen tissue samples from the corpses of 1918 flu victims. Where, you might ask? From Alaska or Norway where bodies may have been buried in permafrost! This makes excellent reading in a new book called "Flu, The Story of the Great Influenza Pandemic of 1918 and the Search for the Virus That Caused It" by Gina Kolata" Click to Check it out.