Centers for Disease Control and Prevention. "Recommended immunization schedules for persons aged 0 through 18 years---United States, 2010." *Morbidity and Mortality Weekly Report*, 8 January 2010. Web. 4 September 2010.

This website provides the most recent recommendations from the Centers for Disease Control and Prevention (CDC) on vaccination schedules for ages 0 through 18 years. The first topic on this website is changes from the 2009 report, which include changes in the poliovirus vaccine, Hepatitis A vaccine, meningococcal conjugate vaccine, and human papillomavirus vaccine. The website then provides charts with footnotes outlining the recommended vaccination schedules. The charts are broken up into two categories: 0-6 years and 7-18 years. Catch-up immunization charts are also provided for persons who start late.

This resource is relevant because it provides an outline of what ages children are receiving vaccinations. However, there are many weaknesses in this resource. The website is vague and provides no explanation for why these vaccines are administered when they are. Additionally, the footnotes for the charts are not easily comprehendible because of the combined use of medical and policy-making language. Some of the vaccinations are only administered when the child is at "increased risk" for a disease, but it does not define what constitutes "increased risk." This source appears to be geared at health care professionals instead of the general public. Overall, this resource is only useful when referencing the recommended vaccine schedule for children, but does not provide any other helpful information on vaccinations.

Whatever Happened to Polio? Smithsonian National Museum of American, 2005. Web. 6 September 2010.

This website was developed by the Smithsonian National Museum of American History. The website contains four major sections: "The American Epidemics," "How Polio Changed Us," "The Virus and Vaccine," and "Polio Today." I focused on the latter two sections of this website. In "The Virus and Vaccine," vaccinations are described as tricking the body's immune system to fight a non-harmful form of the virus. A brief history of the development of vaccinations is also provided which includes Edward Jenner's smallpox vaccine, the first instance of creating artificial immunity. The two types of polio vaccines are also explained: Salk's killed virus vaccine and Sabin's live, attenuated vaccine. The first polio vaccine clinical trials that occurred in 1954 are also mentioned, in which participants were named "polio pioneers." These "pioneers" included 650,000 children who received the vaccine, 750,000 children who received a placebo, and 430,000 children who served as controls. The study was thorough and evaluated both the broad and minute details of the evidence that was recorded, from laboratory procedures to registration methods of the participants. "Polio Today" describes the global campaign of the polio vaccine. National Immunization Days occur worldwide and vaccinate millions of children. World health implications are also discussed. This website also includes a timeline of the history of polio and its vaccine development.

I found this resource to be simple to understand but informative to someone looking for a brief history and explanation of the polio vaccine. The website is not very detailed, but it is a good starting point for gaining a better understanding of the polio vaccine. It is also a good reference for an average person to gain an understanding on

the development of modern vaccines. The website provides many resources that can be further studied in order to get a more in-depth understanding of the topics.

"Vaccines Timeline: 50 Years of Vaccine Progress." *Vaccines & Immunizations*. Centers for Disease Control and Prevention, 19 October 2006. Web. 7 September 2010.

This resource is a timeline published by the Centers for Disease Control and Prevention (CDC) that highlights the major events in the history of vaccinations since the 1950s. The timeline includes when various vaccines were licensed and when policies regarding vaccination in the United States were passed. The timeline begins when the first polio vaccine was licensed in 1955. It ends in 2005 when Rubella was declared to no longer be an epidemic in the United States. The vaccines included on the timeline are polio, MMR (measles, mumps, rubella), Hepatitis B, Haemophilus influenzae type B (Hib), Hepatitis A, Influenza, Acellular pertussis, and rotavirus. Events include governmental policy changes and vaccine recommendations. A particularly interesting event on the timeline is the major resurgence of measles in the United States between 1989 and 1991.

This source provides a good starting point for looking at vaccine history since the 1950s. It is very basic, but it provides the outline that I need to begin researching the history of vaccine development. I do not think that it is detailed enough to provide any pertinent information, but it will provide a good reference for my research. It might also be a good cross-reference to use when matching up dates for big anti-vaccination movements. One of these dates might be when the resurgence of measles occurred. The timeline suggests that the CDC attributed this resurgence to an insufficient number of doses in the schedule by adding another dose shortly after the outbreak. However, this leaves me with the question of whether or not this is the actual cause. Could the resurgence actually be attributed to an anti-vaccination movement?

Meldrum ML. "The historical feud over polio vaccine: how could a killed vaccine contain a natural disease?" *Western Journal of Medicine* 171.4 (1999): 271-3. Web. 8 September 2010.

This is a historical paper published by the History Office of the National Institutes of Health. The paper discusses the historical tension between Salk's killed virus vaccine and Sabin's live-virus vaccine. Both vaccines were developed in the early 1950's. The Salk vaccine was created with the hypothesis that a killed virus could produce the necessary amounts of antibodies to combat the live virus if the body was ever exposed to it. Sabin and his colleagues developed their vaccine with the hypothesis that the live virus would elicit a more natural and effective response. Prestigious scientists and the public refuted Salk's killed vaccine even after successful clinical trials in 1954. Sabin's live virus was recommended and used despite adverse effects, including some cases of polio in vaccinated people. It was not until 1997 that the United States Advisory Committee on Immunization Practices recommended increased reliance on the inactivated poliovirus vaccine. Furthermore, it was not recommended to abandon the oral vaccine until 1999.

This article highlights the public's mistrust in vaccines as early as the 1950's. Although Salk's vaccine was proven scientifically effective, because the public did not understand how it worked, they did not support it. This is an underlying problem in anti-vaccination movements. Lack of understanding of the mechanisms of vaccines can hinder support. In the case of the Salk vaccine, it took over 40 years for the government to recommend increased usage over the live virus vaccine. This short article displays early mistrust of vaccines.

"What's new about the flu vaccine for the 2010-11 flu season?" *Seasonal Influenza.* Centers for Disease Control and Prevention, 10 September 2010. Web. 16 September 2010.

This webpage is under the "Vaccination" section on the Centers for Disease Control and Prevention's (CDC) website concerning seasonal influenza. The website provides information concerning new changes and recommendations on the annual influenza vaccine. The website covers who should get the vaccine, the combination of strains included in the vaccine, and high-risk groups. The website recommends that all persons over the age of six months should be vaccinated against influenza. The 2010 influenza vaccine will be a trivalent vaccine that includes the 2009 H1N1 strain, the H3N2 strain, and the influenza B strain. The website also comments and provides information on vaccines available for persons over age 65, including the Fluzone High-Dose vaccine. Morbid obesity was recently added to the list of those at high risk for complications associated with influenza based on information from last flu season. Other high-risk groups include American Indians and Alaskan Natives. Lastly, the website provides a link in order to find a location to receive the vaccine in the reader's local area.

This website is helpful because it outlines information about the 2010 influenza vaccine. This is the vaccine that we will be questioning about on our survey on student vaccination practices. The website will provide knowledge that will help us develop questions to use on the survey. It is also important to know about the changes from past years' vaccines, including the age expansion. Because this website is intended for the general public, its lack of details is acceptable. The website provides links for further information, which will be useful when exploring the reasons for the changes in recommendations.

"Inactivated Influenza Vaccine: What You Need to Know 2010-2011." Fact Sheet. Centers for Disease Control and Prevention, 19 September 2010. Web. 10 August 2010.

This is a two-page poster, published by the Centers for Disease Control and Prevention, intended to inform the public about the annual influenza vaccine. The poster provides an overview about influenza and information concerning the 2010 vaccine. The poster defines influenza as a contagious disease caused by a virus that is spread through coughing, sneezing, or nasal secretions. Symptoms of influenza include fever, sore throat, chills, fatigue, cough, headaches, and muscle aches. Infants, the elderly, pregnant women, and people with certain health conditions can have worsened symptoms. The poster then defines the two types of influenza vaccines: the inactivated vaccine, which is injected into the muscle, and the live, attenuated vaccine, which is sprayed into the nostrils. All people over the age of six months should receive the 2010 vaccine as early as possible to prevent contracting influenza this season. People with severe allergic reactions to eggs, who have ever been diagnosed with Guillain-Barre Syndrome, or who are moderately or severely sick should wait or not receive the vaccine. The poster provides the moderate and severe risks of the vaccine, but these risks are very rare. More information concerning adverse reactions is provided at the end of the poster.

This poster is helpful because it contains the information that the public is exposed to concerning the influenza vaccine. The poster will aid in forming questions for the survey concerning student practices on receiving the influenza vaccine. The poster contains a lot of the same information as the website titled, "What's New About the Flu Vaccine for the 2010-2011 Flu Season Website." Additionally information includes the risks associated with the vaccine. It also contains more details, making it more useful than the website. The two resources are similar because they were both

published by the Centers for Disease Control and Prevention. The added links on the poster will provide further research materials.

Fiore, Anthony E., Timothy M. Uyeki, Karen Broder, et al. "Prevention and Control of Influenza with Vaccines." *Morbidity and Mortality Weekly Report.* Centers for Disease Control and Prevention, 2010. Web. 19 September 2010.

This website offers a summary of the recommendations of the Advisory Committee on Immunization Practices for the 2010-2011 influenza season. A brief introduction is provided that gives information on the influenza season and virus. The summary then provides the methods that the committee uses to make their recommendations. These methods include discussing newly published studies every two to four weeks. The most recent recommendations were approved in February of 2010, which include expanding the population of who should be vaccinated to all persons over the age of six months, vaccinating children aged six months to two years with two doses of the vaccine, combining three influenza strains into one vaccine, using an alternative vaccine for persons over age 65, and expanding age indications for previously approved inactivated vaccines. After summarizing the changes, the website describes the background and epidemiology of influenza and influenza vaccine efficacy, effectiveness, and safety. Throughout the website, references are provided with supportive studies.

This website is a good resource to start looking at the reasons behind the changes being made to the recommendations for the influenza vaccine. It provides an extensive list of references that the committee has reviewed in their meetings. These references will hopefully provide a clearer picture than what I have found thus far in my research. A negative aspect of this resource is that it would be difficult for the public to understand. It is very detailed and written in a way that would not be easily comprehended by the average American. Additionally, I doubt that the average person reading this website would take the time to read through the references provided.

Jain, S, L Kamimoto, A Bramley, et al. "Hospitalized Patients with 2009 H1N1 Influenza in the United States, April-June 2009." *New England Journal of Medicine* 361.20 (2009): 1935-1944. Web. 29 September, 2010.

This resource is a scientific study that was used as a reference for the CDC's expansion of influenza vaccination recommendations. The study examined 272 patients who were hospitalized for at least 24 hours because of the 2009 H1N1 virus. The virus was confirmed in all patients through a real-time reverse-transcriptase polymerase chain reaction. In the typical influenza season, most hospitalizations occur among persons over the age of 65 years or under the age of two years. This study found that 45% of the patients were children under the age of 18 years, and only 5% were over the age of 65 years. Seventy-three percent of the patients in the study had an underlying medical condition, most commonly asthma, diabetes, heart disease, lung disease, neurological disease, and pregnancy. However, the H1N1 virus also affected young and healthy patients. Seven percent of the patients in the study died, and the median age for those who died was 26 years.

The resource is relevant because it provides scientific evidence for the CDC's expansion of influenza vaccine recommendations. The H1N1 virus affects an unusually large proportion of adults compared to other strains of influenza, which affect mostly the very young and old. However, there are several limitations to the study. Only 25% of the total number of H1N1 cases was represented in the study, and participation was voluntary, thus subject to reporting bias. Additionally, the only patients that were studied had confirmed H1N1, so they may not be representative of all patients with the virus, as most were not tested.

Kumar, A, R Zarychanski, R Pinto, et al. "Critically Ill Patients With 2009 Influenza A(H1N1) Infection in Canada." *The Journal of the American Medical Association* 302.17 (2009): 1872-1879. Web. 1 October 2010.

This resource was another study cited by the CDC in their recommendations for influenza vaccine expansion. It is a similar study to the previous resource but in Canada. It is a retrospective study of 215 intensive care unit patients with confirmed, suspected, or probable H1N1 virus. The mean age of subjects was 32.3 years. Data was collected from several centers using a form distributed to physicians. Comorbidities recorded included congestive heart failure; cerebrovascular, neoplastic, chronic liver or renal diseases; and use of immunosuppressive medication. The most common comorbidities were chronic lung disease, obesity, hypertension, and smoking. Analysis was applied only to the 168 patients with confirmed or probable H1N1. Twenty-nine patients died, four of who were children. Patients who died were more likely to be older or have an underlying medical condition. The study suggests that severe disease and death from H1N1 occurs in relatively healthy adults and adolescents between the ages of 10 and 60 years. This pattern has only been seen previously in the 1918 H1N1 Spanish pandemic.

This study is relevant because it provides a reference of scientific support for the expansion of the 2010-2011 influenza vaccine recommendations, since the vaccine includes H1N1. The study includes a large number of subjects, including both adults and children from racially and geographically diverse backgrounds. However, the study only reflects critically ill patients, excluding patients with less severe reactions to the virus. Additionally, deaths were confined to a certain number of days, so deaths that occurred beyond that range were not recorded. Lastly, although many regions of Canada were represented, most of the cases were from an outbreak in the province of Manitoba, near Winnipeg. The results reflect similar patterns to the previous reference

of H1N1 in the United States, providing stronger evidence for the expanded recommendations.

"Update: Influenza Activity --- United States, August 30, 2009--March 27, 2010, and Composition of the 2010--11 Influenza Vaccine." *Morbidity and Mortality Weekly Report.* Centers for Disease Control and Prevention, 16 April 2010. Web. 3 October 2010.

This resource is the third and final reference of the Centers for Disease Control and Prevention's (CDC) recommendation for expansion. It is a report from the World Health Organization on the CDC's website. The report summarizes influenza activity in the United States during the 2009-2010 influenza season. The majority of influenza activity in 2009 was due to the H1N1 virus. Less than one percent of influenza activity was due to seasonal influenza A (H1), A (H3), and influenza B viruses. In order to characterize influenza strains, states are requested to submit influenza virus isolates to the CDC for antigenic characterization. There were 1,647 influenza viruses analyzed, consisting of two seasonal influenza A (H1N1) viruses, 13 influenza A (H3N2) viruses, 23 influenza B, and 1,609 2009 influenza A (H1N1) viruses. The report also includes the Northern Hemisphere influenza vaccine strain selection based on influenza activity. The recommendations for the vaccine are an A/California/7/2009-like (2009 H1N1) strain, an A/Perth/16/2009-like (H3N2) strain, and a B/Brisbane/60/2008-like (B/Victoria lineage) strain. Other aspects of the report include hospital and mortality rates related to influenza. The editorial note reports that influenza activity increased and remained at higher than normal levels during the spring and summer of 2009 due to the emergence of the 2009 H1N1 virus. It also notes that "vaccination with 2009 H1N1 vaccine remains the key strategy for prevention of 2009 H1N1 influenza infection."

Like the previous two resources, this report gives data to support age expansion of the annual influenza vaccine. It is a strong reference because the data provided relating to active strains of influenza clearly portrays 2009 H1N1 epidemic. It provides

strong evidence to include the strain in the annual vaccine. Combined with the previous two resources, which show that the 2009 H1N1 virus affects young, healthy adults, these resources suggest verification for the CDC's recommendation on expansion of the annual vaccine for all people over the age of six months. The only weakness of this resource is that people without a scientific background may not understand the section on antigenic characteristics of 2009 influenza strains. However, I believe that most people would understand the overall implications of the report.

Reinberg, Steven. "Virtually Everyone Should Get a Flu Shot: CDC." *HealthDay*. 25 February 2010. Web. 5 October 2010.

This is an online news article discussing the recommendation for expansion of the influenza vaccine to all people over the age of six months. The article quotes the Center for Disease Control and Prevention's (CDC) spokesperson Richard Quartarone. In this article, he states that part of the reason that the Advisory Committee on Immunization Practices (ACIP) decided to expand their recommendation was to remove confusion about who needed to be vaccinated. Another reason for expansion is the current H1N1 swine flu pandemic and its effect on a disproportionate number of children and younger adults. This article is the first resource that I have found that includes skepticism on the new recommendations. Dr. Pascal Imperato, an infectious disease expert, claims that expansion does not take into account vaccine production and supply hold-ups that have occurred in the recent past. He makes the argument that when shortages occur, prioritization will inevitably result.

This article is relevant because it is an example of media attention relating to the expansion of recommendations of influenza vaccines. This is the first resource that uses the removal of public confusion concerning recommendations as a reason for expansion. I found this interesting because while a spokesperson for the CDC supplies this reason, it is not reported in any of the CDC reports as a reason. This makes me wonder what else was not reported from the ACIP weekly meetings. This article is also the first reference that provoked me to question the CDC and its recommendations, providing a starting point to research further into what else may not be officially reported by the CDC.

Prifti, Christine. "The Vaccine Industry: An Overview." *VaccineEthics.org*, 2010. Web. 7 October 2010.

This is a website that I found while looking for skepticism on the expansion of the Centers for Disease Control and Prevention's (CDC) recommendations for the influenza vaccine. The website provides information about the vaccine industry. According to the website, four companies control 80% of the vaccine market worldwide, opposed to 35 companies 30 years ago. These companies include GlaxoSmithKline, Merck, Novartis, Sanofi Pasteur, and Wyeth. The reason for this decrease is because other pharmaceuticals make more profit than vaccines do. Vaccine production requires 12-15 years of research and between 500 million and 1 billion dollars. While the production is costly and time consuming, a single vaccine is usually a one-time use. Thus, vaccines require a large market in order to be profitable. The website also states that the government is the largest single purchaser of vaccines.

This article is relevant to our research because it provides information about the vaccine industry, which is a topic I have not previously researched. It offers insight on why the CDC might want to expand influenza recommendations in order to make a larger profit, as vaccines are typically not high profit pharmaceuticals. My first concern about this website was that it was not reliable. However, the article cites scientific references, and the website is maintained by the University of Pennsylvania Center for Bioethics and supported from a grant from the Greenwall Foundation. The websites provide many links that I think will be useful in the future. These links include over 1300 references on vaccine ethics, policy, and history. Overall, the website provided a good starting point to research the vaccine industry and will supply beneficial resources for future data.

Salinsky E, Werble C. "The Vaccine Industry: Does It Need a Shot in the Arm?" *National Health Policy Forum*, 2006. Web. 13 October 2010.

This resource is a paper that was published in 2006 by a nonpartisan research and public policy organization at The George Washington University. The article is 34 pages in length, but I focused on the area that reported on the vaccine market. The paper highlights the negative aspects of the market and the reasons behind its lack of success. Currently, vaccinations account for only 1.5% of all pharmaceutical revenues. However, the market has been slowly growing since 1992 due to worldwide efforts to eradicate polio, the introduction of new pediatric vaccines, and improvements to existing vaccines. The article hypothesized that by 2010, there would be thirty new vaccines added to the market. The vaccine market is suffering for several reasons. One of which is the fact that a vaccine is only used a limited number of times in a persons lifetime. This contrasts with "blockbuster" drugs, such as Lipitor, that are filled 66 million times each year. This combined with a low growth market creates a lack of investment in vaccine development. Additionally, 60% of vaccine production costs are fixed; they do not change no matter how much product is produced. This high fixed rate cost combined with the perishable nature of vaccines causes manufacturers to attempt to closely match production with demand. However, this can lead to vaccine shortages, especially with the influenza vaccine because it changes annually, the production process is not predictable, and reserves cannot be established.

This article goes into more depth about the shortcomings of the vaccine industry. It is a very informative article and relatively easy to read and comprehend. Furthermore, it is nonpartisan, so I do not feel that it is biased. I do not see any weaknesses in the article. Reading about the high fixed rate costs make me question the recommendation for expansion by the Centers for Disease Control and Expansion.

When there is a larger demand for a vaccine, there is an increase in production volume. This leads to a decrease in production costs, and thus a decrease in prices. The government buys 60% of vaccines, so it would favor a lower cost. This is an issue that the article provides that I would like to research further.

"60 Minutes: An Inside Look at H1N1 Vaccine Production." Online Video Clip. *60 Minutes*, 1 November 2009. Web. 14 October 2010.

This resource is an online clip from a *60 Minutes* episode that aired on November 1, 2009. The clip was aired during the beginning of the 2009 H1N1 outbreak. By the time the segment was aired, H1N1 was widespread in 48 states and the government had funded $3 billion for the production of a vaccine. The segment opens with Luke Duvall, who has been breathing with the help of a ventilator for the past 17 days because of an adverse reaction to the virus. The camera then cuts to a video showing the lines of people in Duvall's hometown waiting for their H1N1 vaccine, highlighting the shortage of vaccine that the country faces. The segment provides a simple explanation on how the vaccine is produced while showing clips of the $250 million dollar facility where it is manufactured. The host of the program discusses the public skepticism toward the vaccine. According to the segment, 40% of those polled would not take the vaccine, and the 1976 outbreak of Guillain-Barre Syndrome is mentioned as one of the reasons. At the time of the clip, there were fewer than 200 reports of side effects. The segment closes with Luke Duvall again, struggling to breath and equipped with a feeding tube in his nose.

This video clip is relevant to our research because it provides an example of how the media portrayed H1N1 during the early stages of the 2009 outbreak. However, it seems like a classic example of the media attempting to dramatize a scenario, by both opening and closing the segment with an extreme case and further scaring the viewers by highlighting the shortage of the vaccine. Overall, this video is interesting to analyze media involvement in health issues, but not very helpful for our research, as the unbiased information seems watered down for our knowledge, and the remainder of the segment seems biased.

Stratton, Kathleen, Christopher B. Wilson, and Marie C. McCormick, eds. *Immunization Safety Review: Multiple Immunizations and Immune Dysfunction.* Washington, D.C.: National Academy Press, 2002. Print.

This is a book published by the Institute of Medicine concerning the relationship between multiple immunizations and immune dysfunction. The Institute of Medicine is an independent organization that works outside of the government to provide unbiased advice to decision makers and the public. The book provides a review of evidence relating to the hypotheses that multiple immunizations increase risk for immune dysfunction, specifically type 1 diabetes and asthma. For each hypothesis, the committee provided both a scientific assessment (epidemiological evidence, clinical evidence, and biological mechanisms) and a significance assessment (burden of health risks and level of public concern). In the scientific assessment regarding causality, the committee concluded that the epidemiological and clinical evidence favor rejection of a causal relationship between multiple immunizations and increased risk of heterologous infection and type 1 diabetes. However, they concluded that the evidence was inadequate to come to a decision concerning a causal relationship between multiple immunizations and an increased risk of allergic diseases, specifically asthma. The biological mechanisms examined are summarized clearly in a chart that I included in my research notebook. They range from theoretical only to strong in weight. The committee's significance assessment determined that the concern for multiple immunizations has been, and could continue to be, significant in terms of parental worries, potential health burdens, and future challenges for policy-makers. The committee does not recommend a policy review of the current vaccination schedule or any of the currently licensed vaccines. Because of the complicated nature of this information, I am providing a bulleted summary of the previous information:

- Clinical and Epidemiological Literature-multiple immunizations do not lead to risk of infection or type 1 diabetes; possible role in the risk of allergy is indeterminate
- Biological Mechanisms Literature-the evidence that immunization might lead to infection, autoimmune disease, or allergy is more than only theoretical (refer to chart for specific examples)
- Recommendation of limited but continued public health attention
- No recommendations for policy change

Overall, this is an extremely useful resource for our research relating to the scientific aspects of multiple vaccinations and immune dysfunction. The book provides unbiased evidence and many references of peer-reviewed journal articles that can be further researched by the team in the future. The summary provided in the beginning of the book provides a useful and quick reference, but a more in-depth explanation is provided following the initial summary. There are also easy to comprehend charts, some of which are included in my notebook. The only weakness of this resource is that it is somewhat difficult to comprehend due to the language, but because it provides summaries and supplemental material that are easier to understand, it remains a very strong resource.

Vellozzi, Claudia, Karen R. Broder, Penina Haber, et al. "Adverse Events Following Influenza A (H1N1) 2009 Monovalent Vaccines Reported to the Vaccine Adverse Event Reporting System, United States, October 1, 2009-January 31, 2010." *Vaccine* 28.45 (2010): 7248-7255. Web. 9 November 2010.

This study examines reports of adverse events following vaccination with the first 2009 H1N1 vaccines by analyzing the Vaccine Adverse Event Reporting System (VAERS). Special attention was paid to reports coded as serious and any reports that were indicative of Guillain-Barre Syndrome or anaphylaxis. The study found that the number of reports of adverse events was higher following the 2009 H1N1 vaccine as compared to following the 2009-2010 seasonal influenza vaccination. The most frequent adverse event categories were neurological and respiratory. There was no pattern that would suggest a causal relationship between the vaccine and death. Although the number of reported adverse events was higher than in previous seasonal influenza vaccines, the paper concluded that the 2009-H1N1 vaccinations did not result in a significant general increase in serious adverse events.

The study is relevant to our research because it examines the relationship between the H1N1 vaccine and adverse events. The numbers presented in the study could provide evidence for those who do not the vaccination. However, the paper contradicts these numbers through a thorough discussion of the limitations of the study and why, despite the increased reports, it concludes that there are no safety concerns with the vaccine. The raw figures in this study are skewed by the publicity that surrounded the vaccine and the efforts to increase reporting to the VAERS. These factors contributed to more than a three-fold increase in visits to the VAERS compared to previous influenza seasons. Once these limitations were accounted and adjusted for, the findings following the 2009-H1N1 vaccines were similar to the findings from a fifteen-year review of reports following receipt of previous influenza vaccines.

Although the conclusions are justified, because of all the other limitations that were listed, I am hesitant to believe that this is a strong reference.

Israeli, Eitan, Nancy Agmon-Levin, Miri Blank, et al. "Guillain-Barre Syndrome—A Classical Autoimmune Disease Triggered by Infection or Vaccination." *Clinical Reviews in Allergy and Immunology* [Epub ahead of print] (2010). Web. 10 November 2010.

This paper is a review of Guillain-Barre Syndrome (GBS), its causes, and the hypotheses regarding the biological mechanisms relating to the disease. The paper defines GBS as a "disorder in which the immune system attacks gangliosides on the peripheral nervous system" (1). There are several forms of GBS and it involves both genetic and environmental factors, which may be triggered by infections or vaccinations. GBS is categorized as an autoimmune disease mediated by anti-ganglioside antibodies. Approximately one-third of all cases of GBS are preceded by the bacterium, *Campylobacter jejuni.* This bacterium expresses a molecule that mimics gangliosides present in peripheral nerves. This has led to the hypothesis of molecular mimicry as a biological mechanism for the onset of GBS. In 1976, the increase in incidence of GBS following the "swine flu" vaccine suggested that the increased incidence was related to the vaccine. One hypothesis for this was that the vaccine was contaminated with *C. jejuni* antigens or that other vaccine components induced an anti-ganglioside antibody response in susceptible persons. *C. jejuni* was not found in the vaccine, but the vaccines did induce anti-ganglioside antibodies in mice. The cause of this induction remains unknown.

I found this paper to be very helpful in elucidating one of the biological mechanisms behind vaccination and autoimmunity, molecular mimicry. By understanding this mechanism, supporters of the anti-vaccination movement can gain scientific evidence for their cause. However, the authors also discuss the lack of epidemiological evidence for a relationship between influenza vaccination and autoimmunity, with the exception of the 1976 incident. The only flaw of this paper is that parts of it are extremely difficult to understand without a background in immunology, which I do not have. The other sections of the paper make up for this confusion by providing clear summaries. A question that I have after reading this study is: Why does the cause of induction of anti-ganglioside antibodies from the 1976 H1N1 vaccine remain unknown?

Schessl, Joachim, Birgit Luther, Janbernd Kirschner, et al. "Infections and Vaccinations Preceding Childhood Guillain-Barre Syndrome: A Prospective Study." *European Journal of Pediatrics* 165.9 (2006): 605-612. Web. 10 November 2010.

This paper focuses on children with Guillain-Barre Syndrome (GBS) in Germany, Switzerland, and Austria. It examines the prior infections and vaccinations of the children by studying stool, serum, and cerebrospinal fluid samples for evidence of bacteria and viruses. Ninety-five children were included in the study over a period of forty months. In 82% of participants, preceding events were reported. In 70-80% of children who developed GBS, acute infections were present within a four to six week

period prior to onset. The most common agents found in the samples from the subjects were Coxsackieviruses (15%), *Chlamydia pneumoniae* (8%), cytomegalovirus (7%), *Mycoplasma pneumoniae* (7%), and *Campylobacter jejuni* (7%). This pattern is unlike adults, in whom the most frequent triggering agent for GBS is *C. Jejuni.* Only eight of the children had been vaccinated during the six weeks preceding the onset of GBS, and in six of these children, a concomitant infectious disease was reported. There was no association between the type of prior infection and the symptoms and severity of the disease.

Overall, this is a good resource because it examines relationships that have not previously been examined. It is relevant to our research because parents who are concerned about their children, not about other adults, lead most of the anti-vaccination movement. However, there are some limitations to the study. There is no control group that could prove that these findings lead to a specific relationship with GBS. A sufficient control group would be age and gender matched. This data is also difficult to compare to other literature because there is no other relevant literature published. This paper leaves me with the question of why the causes of GBS onset seem to be different in children and adults.

Yoo, Wan-Hee. "Adult Onset Still's Disease Following Influenza Vaccination." Letters to the Editor. *Joint Bone Spine* 77.4 (2010): 366-375. Web. 16 November 2010.

This is a case study that was featured in the "Letters to the Editor" portion of *Joint Bone Spine.* The patient presented is a 73-year-old women who developed daily high spiking fever, sore throat, and polyarthritis of both hand, wrist, and knee joints, without skin rash two days after receiving the inactivated influenza vaccine. The diagnosis of Adult Onset Still's Disease (AOSD) was made based on the criteria. There was no previous evidence of the influenza vaccine causing rheumatic diseases at the

time of publication, but there had been several case reports documenting possible relationships. The cause of AOSD is unknown, but triggering factors include influenza A, parvovirus B19, cytomegalovirus, parainfluenza, rubella, and coxsackie B4. The mechanism by which the disease is triggered is unclear but may involve episodes of over activity of inflammatory responses, molecular mimicry, induction of synthesis of autoantibodies, production of cytokines, or Th1/Th2 lymphocyte imbalance. The relationship between the influenza vaccine and AOSD is unknown.

This case review is relevant to our research because it provides an example of the development of an autoimmune disease after receiving the influenza vaccine. However, the paper only presents one patient and does not provide many details regarding the etiology of the disease. For the most part, the etiology appears to be unknown. This paper provides evidence for the anti-vaccination movement because it provides an example of an adverse reaction following vaccination that cannot be explained by the scientific community. However, deeper interpretation provides evidence that supports vaccination because a relationship between the influenza virus and AOSD is cited.

Mantadakis, Elpis, Evangelia Farmaki, Stavros Thomaidis, et al. "A Case of Immune Thrombocytopenic Purpura After Influenza Vaccianation: Consequence or Coincidence?" *Journal of Pediatric Hematology/Oncology* 32.6 (2010): 227-229. Web. 17 November 2010.

This resource is another case study of a patient developing an autoimmune disorder after receiving the seasonal influenza vaccine. The patient described is a previously healthy 3-year-old boy who developed immune thrombocytopenic purpura (ITP) 26 days after receiving the second dose of seasonal influenza vaccine. The influenza vaccine has rarely been linked to development of thrombocytopenia, a

condition in which the immune system destroys its own platelets. There are no epidemiological studies that find a significant relationship between the vaccine and thrombocytopenia or ITP. There have, however, been reports of a relationship between the influenza virus and thrombocytopenia. In one study, 38.7% of hospitalized children with H5N1 developed thrombocytopenia. The most likely mechanism for this is through virally induced molecular mimicry. Young children especially have a higher likelihood of autoimmunity because their idiopathic network is still forming.

This resource is relevant to our research for two reasons. On the surface, it provides the anti-vaccination movement with a case of autoimmunity post-vaccination in a young child. However, upon reading the entire study, it actually provides stronger evidence to receive the influenza vaccine, as ITP is more likely to be induced from the virus, not the vaccine. This is also the case with the previous resource relating to Still's Disease. The study is limited because there is not sufficient literature on vaccine-induced ITP to compare it to. Moreover, the literature related to influenza-associated ITP is limited because most patients do not have severe enough symptoms to receive medical attention. This lack of resources hinders our ability to research this topic further.

Plasencia, Z. Mendoza, M. Gonzalez Lopez, M.L. Fernandez Sanfiel, and J.R. Muniz Montes. "Acute Disseminated Encephalomyelitis with Tumefactive Lesions After Vaccination Against Human Papillomavirus." Letters to the Editor. *Neurologia* 25.1 (2009): 58-69. Web. 19 November 2010.

This resource is a third case study of a previously healthy 17-year-old female who presented with Acute Disseminated Encephalomyelitis (ADEM) 15 days after the second administration of the Gardasil series. ADEM is an autoimmune disease diagnosed through MRI by multiple, asymmetrical, supratentorial and infratentorial hyperintense lesions. Gardasil is a vaccine prepared from virus-like particles, which

cannot infect cells, reproduce, or cause disease. Prior to its approval, there were no reports of adverse neurological effects, but there have been cases reported linking the vaccine to Guillain-Barre Syndrome and other cases of headache and dizziness. In 2008, 5 Australian patients presented demyelinating syndromes of the central nervous system within 21 days of the second or third dose of Gardasil. Only one other case of ADEM was published after receiving the second dose of Gardasil.

This paper is relevant to our research because it describes a case of autoimmunity after vaccination in an adolescent. This case, however, is different from the previous cases because it focuses on the Gardasil vaccine, not the influenza vaccine. The paper is high impact because the disease causes brain lesions, even though the disorder can be treated. Although this is only the second reported case of ADEM after Gardasil, it can provide clinical and scientific evidence for the anti-vaccination movement. It also contributes to the public skepticism of Gardasil since it is a relatively new vaccine.

Balofsky, Ari, Nancy Agmon-Levin, and Yehuda Shoenfeld. "The New H1N1 and HPV Vaccines and Old Fears." *Current Opinion in Rheumatology* 22.4 (2010): 431-436. Web. 22 November 2010.

This is a review of the literature concerning the recent H1N1 and human papillomavirus vaccines. The first section of the review provides examples of several studies that describe autoantibody induction, autoimmune phenomena, and autoimmune disease after the receipt of a vaccination. The most common reports include arthritis, neuropathy, encephalitis, vasculitis, and demyelination. Despite these studies, it is difficult to define a causal relationship between autoimmunity and prior

vaccination because the studies are not large enough to be significant, and the cases that are documented contain limitations. The next section of the paper describes the mechanisms of autoimmunity that vaccinations could possibly trigger. The most likely mechanism is molecular mimicry of the infectious antigen to self-antigens. The paper also discuses adjuvants in the vaccines, which are added in order to increase antigen recognition and desired immune response. In the discussion of the H1N1 vaccine, the 1976 Guillain-Barre Syndrome outbreak is noted because the vaccine component responsible for producing the response was never confirmed. The HPV vaccine section of the review discusses the two approved vaccines: Gardasil and Ceravix. Gardasil uses one adjuvant, while Ceravix uses two. At the time of the review there were 60 studies of autoimmune disorders associated with these vaccines, 51 with Gardasil alone. The paper concludes that the actual relationship between vaccines and autoimmune phenomena is extremely difficult to confirm.

This paper is relevant because it provides a fairly simple summary of current literature regarding new vaccines and autoimmunity. It also provides more insight into the biological mechanisms behind this phenomena and is the first resource that discusses the possible role of adjuvants in autoimmunity. Some of the language is difficult to understand, but overall, the resource is relatively easy to comprehend and provides other studies as references that can be studied further. A disclosure was included at the end of the review stating that one of the authors appeared in court on the issue of vaccine-induced autoimmune conditions. When I researched this further, I found that Shoenfeld testified on behalf of a boy who experienced autoimmunity after vaccination.

Koenig, Helen C., Andrea Sutherland, Hector S. Izurieta, et al. "Application of the Immunological Disease Continuum to Study Autoimmune and Other Inflammatory Events After Vaccination." *Vaccine* [Epub ahead of print] (2010). Web. 24 November 2010.

This paper proposes a new classification system to identify associations between vaccines and immunological reactions. The current system uses a system-organ classification and umbrellas all inflammation against self as "autoimmunity." The authors argue that this type of classification causes diminished ability to detect true association. The proposed system is based on the mechanistic classification of inflammation against self, using a continuum of a full range of immunologically

mediated events. The paper then describes each of these events and the mechanisms by which vaccines could theoretically induce them. The events described include classical autoimmune diseases in relationship to vaccine responses, innate immune-mediated reactions related to adjuvants, immune complex deposition diseases, allergic reactions, molecular mimicry as a mechanism of vaccine-induced autoimmunity, and MHC class 1-associated intermediate diseases—between innate and adaptive immunopathology, and genetic predisposition. The authors believe that their classification system will provide a more accurate system for evaluating potential associations between vaccines and immune-mediated events.

This paper is relevant to our research because it describes many possible mechanisms for immune reactions after vaccinations. Although the paper's intent is to propose a new classification system, it provides a lot of information to help understand the way vaccinations might react with the body. Even without a strong background in immunology, I could begin to understand these different mechanisms. A limitation of the reference is that there is some overlap between the different categories, which makes the classification more complex. However, this limitation is not relevant in our use of the article. This would be an excellent paper to reference when trying to understand the various mechanisms of vaccine interaction with the body.