The New England BEACON

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IMMUNIZATIONS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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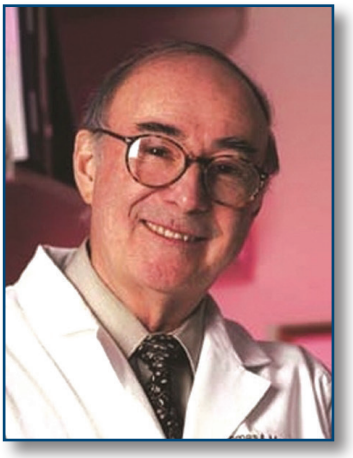

There is a recognized increased risk of infections in patients with systemic sclerosis (SSc) even when they are not receiving treatment. This statement applies to both bacterial and viral infections and to both usual (common) and unusual (rare) infections. The reason for this susceptibility is that SSc patients have an abnormal immune system which may not be able to respond in a coordinated and effective way when the patient is exposed to infectious agents. The risk is magnified when SSc patients are taking medications that suppress the immune response, such as corticosteroids or immunosuppressive agents (mycophenolate mofetil, cyclophosphamide, methotrexate).

Several studies have concluded that less than 40% of persons with various types of arthritis (rheumatoid arthritis and psoriatic arthritis) receive the most common immunizations, such as the influenza (flu) vaccine or Pneumovax, which is directed against "pneumococcus," the most frequent bacterial cause of pneumonia. Similar results have been found for scleroderma. A French group published in 2010 that less than 40% of 177 SSc patients received flu vaccine during one calendar year.

The reasons for low immunization rates in patients are several, including (1) patients' fear of side effects; (2) patients not having adequate information such as reminders from the physicians and (3) physicians' prejudices. Patients are concerned that they may get the disease for which they are being vaccinated (flu, pneumonia) from the vaccine, that their SSc may worsen, or that they might infect others (family members, friends). Physicians sometimes believe that vaccines are ineffective in SSc and other connective tissue disease (CTD) patients or that "live" viruses may be dangerous.

There are two important aspects to consider about vaccines. First, to distinguish between "recall" and "neo-" immunizations. Recall refers to a "booster" vaccine. The person has previously had the infection and developed immunity at that time. The goal of recall vaccination is to "boost" or increase existing antibody levels. A "neovaccination" is given to persons who have never had the infection in question and therefore have no immunity. The

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PATIENT EDUCATION SEMINAR 2014

Carol Feghali-Bostwick, MD

SFNE's biennial Patient Education Seminar will be held on Saturday, April 5, 2014 at the Boston Marriott Peabody. Featured speakers will include Dr. Carol Feghali-Bostwick and Dr. Philip Clements. There will also be a speakers' panel to address several common scleroderma issues.

Registration information is on page 9, and you can register online or by sending in the registration form with payment. Morning snacks and a luncheon are also included.

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goal in this instance is to develop antibodies to prevent further infection.

Another important consideration is whether the vaccine contains "live" or "killed" organisms. Live organisms are capable of reproducing and causing infection. "Attenuated" is a term used for living organisms which are inactivated and thus not capable of producing or causing infection. In contrast, "killed" organisms are components of organisms which are made synthetically (in a test tube) which can mimic the organism and cause the human body to make appropriate antibodies.

Table 1: Vaccines Available

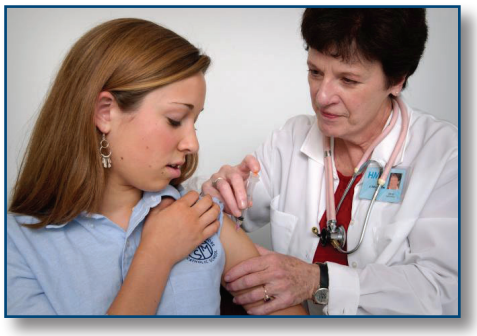
Entirely Safe
(Killed or synthetic)

1. DPT (diptheria, pertussis, tetanus) - childhood
2. Flu and H1N1 flu by injection
3. Hepatitis A/B
4. Human Papilloma Virus (to prevent cervical cancer)
5. Anthrax
6. Pneumovax
7. Menigococcus (to prevent a type of meningitis)
8. Hemophilus influenza - childhood
9. Typhoid

Most often but not always safe
(Live or attenuated)

1. Herpes zoster (shingles)
2. Nasal flu
3. Measles, mumps, rubella (MMR)
4. Yellow fever
5. Oral polio

There is a long list of vaccines which are considered by experts to be "entirely safe" (Table 1). They include the common vaccines that primary care physicians urge all persons to receive, including flu, Pneumovax, and hepatitis A and B vaccines. There is a group of live/attenuated viruses used in vaccinations which could conceivably cause disease in the recipient if that individual is



immunosuppressed. They include the shingles virus, nasal flu virus, measles /mumps /German measles and oral polio (Table 1). A theoretical problem with live virus vaccines is that viral particles can be "shed" to other persons in close contact with the vaccine recipient. One study suggested that this type of viral spread to another individual with resulting disease is very low (less than 1%) and occurs almost exclusively if the "other" person is himself/herself an autoimmune disease or CTD patient on immunosuppressive treatment or otherwise severely immunocompromised, for example having HIV/AIDS or a transplant recipient on anti-rejection drugs.

A vaccine recently available about which there has been considerable discussion is the shingles vaccine. Shingles is the result of reactivation of the chicken pox virus which can remain dormant for many years in nerve tissue. Activation leads to a rash consisting of fluid-filled "blisters" and severe pain along the course of the nerve. Pain may persist long after the rash subsides. The dormant virus can become activated under certain conditions such as older age, CTD, immunosuppressive drugs, or other "triggers."

The purpose of the vaccine is recall – to boost immunity. A concern has been the possible development of shingles in the recipient after vaccination. In a Medicare study, 633 patients were vaccinated and there were no cases of shingles identified during a seven week follow-up period. Another study suggested that the shingles vaccine is safe in patients receiving immune suppressive drugs in "standard" doses, including prednisone less than 20mg/day, methotrexate doses used for treatment of rheumatoid arthritis, and Imuran. There are limited data for other drugs such as CellCept. Rheumatologists do not advise receiving the shingles vaccine if a patient is taking "biologic" agents such as Cytoxan, Rituxan, Enbrel, Remicade, Orencia, etc.

Some immunizations are recommended for persons traveling to areas of the world where certain infections are extremely common in the population. An example is the yellow fever vaccine (neo-, live virus). The advice of a foreign travel infectious disease specialist may be necessary regarding receiving this vaccine if a patient is immunosuppressed. One possibility to maximize the likelihood of a successful vaccination is to stop the immunosuppressive drug(s), wait four weeks, immunize, then wait for an additional four to six weeks for proper antibody production to occur. This time period is an estimate – there are no available guidelines. You and your rheumatologist will have to discuss whether or not you will be able to be off your immunosuppressive

medications for eight to ten weeks without a disease "flare-up."

As noted above, there has been concern that CTD patients may not develop adequate immunity after vaccinations. This is probably correct, as most studies show lower than ideal post-vaccination antibody levels in CTD patients. For example, good antibody levels may result in 75-90% of normal persons, 60-80% in CTD patients, and 50-70% in CTD patients on prednisone and/or immunosuppressive drugs. Even with lower antibody levels, immunity to infections may be improved because other parts of the immune system may be "strengthened" by immunization. Thus, the standard recommendation is "If it is safe, immunize." There are three published studies which focus specifically on SSc patients receiving the flu vaccine or Pneumovax (Table 2). The bottom line is that they are both safe and reasonably effective vaccines.

I draw the following conclusions from my reading and my personal experiences.

(1) Vaccines are important in preventing bacterial and viral diseases.

(2) Vaccines in CTD patients are under-prescribed by physicians.

(3) In general, vaccines are extremely safe.

(4) Immunizations are somewhat less effective in stimulating antibody production in CTD patients but also may be protective by stimulating other parts of the immune system.

(5) Regardless, vaccinations should be given to CTD patients, particularly those at increased risk for bacterial or viral infections.

(6) All patients on immunosuppressive drugs with scleroderma should receive the flu and pneumonia vaccine. The shingles vaccine should be discussed with their doctor.

(Reprinted with permission from the Winter 2013 UPMC & University of Pittsburgh Collagen Connection Newsletter)

Table 2: Vaccination Studies in Systemic Sclerosis

Author (Year)	Vaccine	Patients	Results
Setti (2009)	flu	46	Antibody protection increased from 50% before to 90% after; no patients had worsening of SSc
Litinsky (2012)	flu	26	Antibody levels increased in most patients; lower response in SSc patients with lung disease; no change in measures of disease activity
Mescado (2009)	Pneumovax	16	80+% developed protective antibody levels; same results in SSc subtypes (diffuse, limited) and in patients taking or not taking immunosuppressive drugs

PRODUCTS THAT HELP

Oxy Couture, LLC is a company that has developed a nasal cannula cover (for patients who need oxygen) that is washable and interchangeable. These covers are designed to aid in the prevention of breakdown in the skin from the tubing due to prolonged oxygen wear.

The covers are made of preshrunk, 100% combed cotton that is micro sanded for a luxurious feel. They come in many styles and can even be customized.

You can find out more about this inventive product at *www.oxycouture.org*. We would like to thank North Shore Support Group Leader Roberta Mauriello, who alerted us to this product.

"Don't think outside the box... Think like there is no box."
~ Unknown~