University of Saskatchewan
MDIBDC
Multidisciplinary Inflammatory Bowel Disease Clinic

Inflammatory Bowel Disease: Immunizations

Introduction

In Inflammatory Bowel Disease (IBD) the body's immune system attacks the intestinal walls by producing inflammation. This inflammation accounts for the various symptoms and complications of IBD. While there has been no cure discovered so far, many medical advances have been made in controlling the inflammation. These medications improve symptoms and decrease development of complications which may lead to surgery or hospitalization.

Despite having more inflammatory activity in IBD, the disease itself can lead to a compromised, or weakened, immune system. The reasons for this are not completely understood but may include malnutrition, chronic inflammation and altered immune function. In addition, most of the medications used to control IBD work by suppressing the immune system in different ways. This combination can leave the IBD patient more vulnerable to infections. In one study of over 6000 patients, 7.7% of participants developed a serious infection within 5 years[1]. Those with more severe disease activity, and requiring stronger medication, were at higher risk. For this reason, immunizations are an important preventative measure in optimizing health. Multiple international organizations have created guidelines for immunization in patients with IBD, and the goal of this document is to summarize these recommendations.

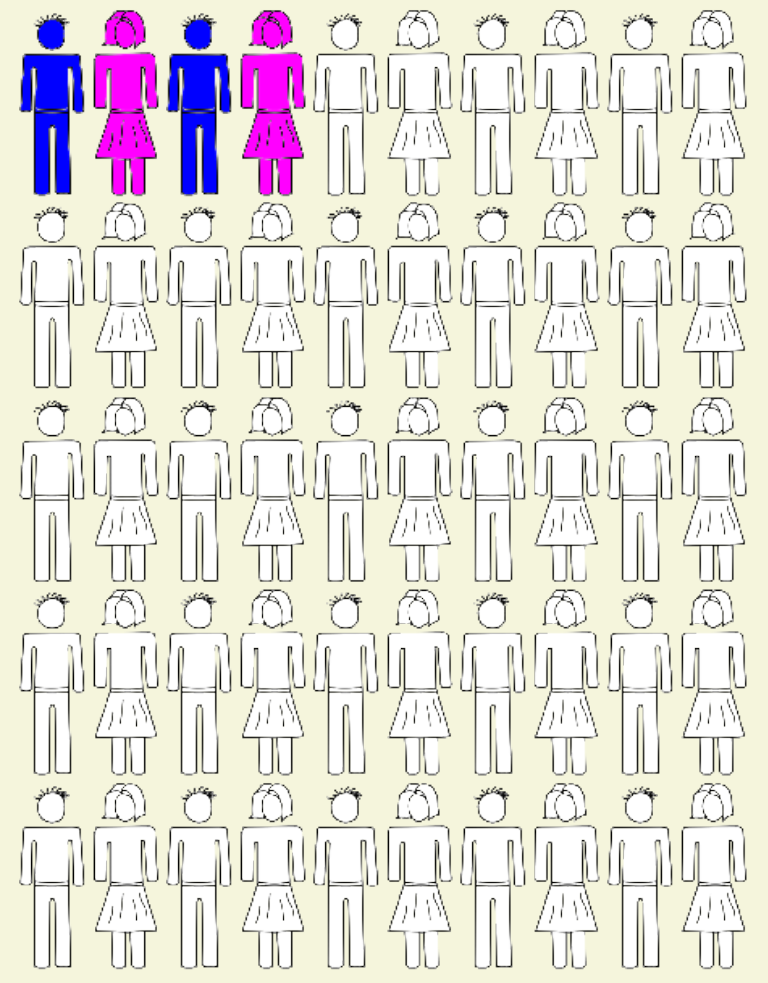

Fig 1: In a follow-up of over 6000 IBD patients for 5 years, about 8% (e.g. 4 out of 50) developed a serious infection. Patients taking an anti-TNF agent were at a slightly higher risk compared to those who did not.

Recommended Immunization Summary

The following immunizations are recommended in all IBD patients (see text & table 1 for details):

- Influenza
- Pneumococcal
- Hepatitis B
- Tdap: Tetanus, Diptheria, Acellular Pertussis

The following are recommended in appropriate circumstances (see text & table 1 for details):

- HPV vaccine: Human Pappiloma Virus
- Meningococcal
- Hepatitis A
- Varicella (Chicken Pox) & Zoster (Shingles)
- MMR: Measels, Mumps, Rubella

When Is My Immune System "Weakened"?

Having a weakened immune system is referred to as being immunocompromised or immunosuppressed. The immune system is thought to be weakened if any of the following are true[2]:

- Steroid use (>20mg/day prednisone for two or more weeks)
- Azathioprine (Imuran) therapy
- Methotrexate therapy
- Anti-TNF therapy (e.g. Remicade, Humira)
- Significant malnutrition

If any of the above medications are stopped, the immunosuppressive effect is thought to carry on for three months. Treatment with 5ASA medications (e.g. Salofalk, Asacol, Pentasa, Mesalamine, Sulfasalazine) does NOT result in a weakened immune system as these medications are anti-inflammatories (not immune suppressants).

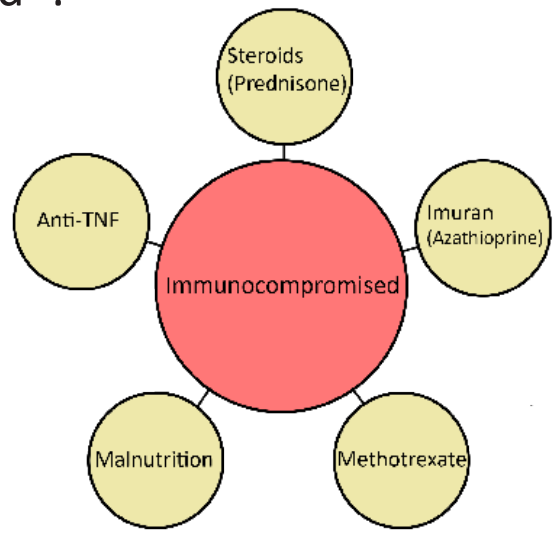

Fig 2: Causes of immunosupression

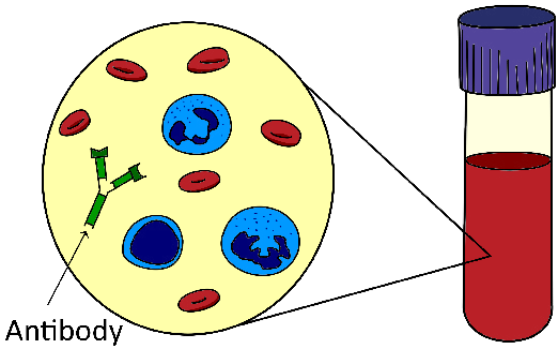

Fig 3: Specific antibodies may be produced from previous exposure to a disease or from the specific immunization. These can be detected with a blood test (titre check).

What Is a Titre Check?

Antibodies help your immune system fight infection. For certain diseases, prior vaccination or exposure to the disease may have already resulted in immunity. This can be checked with a blood test which looks for specific antibodies that the immune system produces. If the antibodies are absent, there is no immunity (ie. no protection). This type of check can be done with Hepatitis A, Hepatitis B, Measels, Mumps, Rubella and Varicella. It can be useful if someone does not recall whether they had a particular vaccine.

What Is the Difference Between Live Attenuated and Killed/Inactivated Vaccines?

A live attenuated vaccine uses a weakened form of the virus to stimulate the body's immune system. Killed/inactivated vaccines do not use a weakened form, but rather only surface parts of the virus or bacteria to stimulate

an immune response. Live attenuated vaccines are safe in the general population, but a theoretical risk of the vaccine causing illness in someone with a weakened immune system exists. For this reason, live attenuated vaccines are not recommended for patients who are immunosupressed. Live attenuated vaccines include the MMR, Varicella and Zoster vaccines. Killed/inactivated vaccines do not carry this risk.

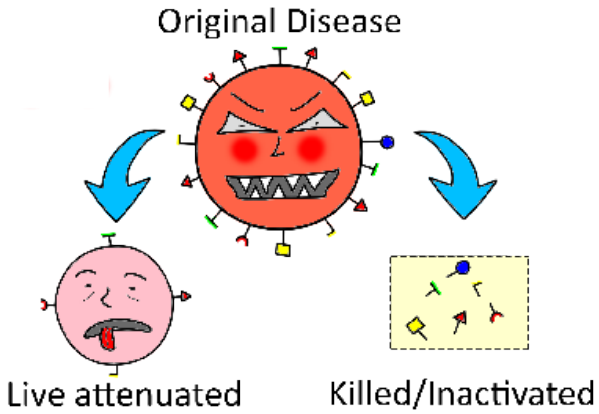

Fig 4: A live attenuated vaccine is a weakened form of a virus. Killed vaccines only use surface components of a virus. Both allow your immune system to build immunity, but live attenuated vaccines should not be given if someone has a weakened immune system.

More About Specific Immunizations

Influenza

Influenza is an air-borne virus that infects the respiratory (lung) cells. It results in the 'flu' and is one of the causes of pneumonia. Pneumonia is the most commonly cited serious infection in the TREAT registry, which is a set of closely followed IBD patients.[1] An annual influenza immunization is recommended for all patients with IBD. In those who are taking immunosuppressive medication, only the inactivated vaccine should be used.

Pneumococcal

Streptococcus pneumoniae is a bacterium which can infect the lung (causing pneumonia) or brain (causing meningitis). Immunization is recommended and involves a onetime dose with a 5-year booster for all patients.[2-4] It is an inactivated vaccine and can therefore be given at any time, regardless of current immunosuppressant regimen.

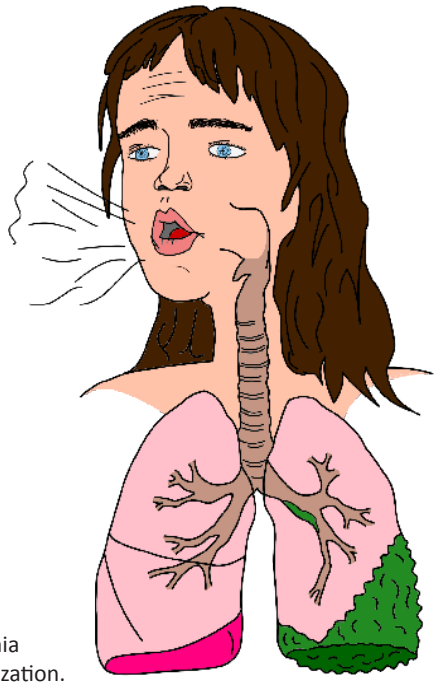

Fig 5: One of the most common infections among IBD patients is pneumonia (lung infection). Some types of pneumonia can be prevented with immunization.

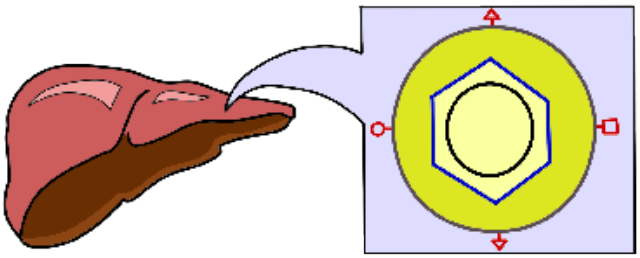

Fig 6: Hepatitis B infection usually has no symptoms until the disease is very advanced. Treatment with Anti-TNF agents can result in a severe worsening if someone is carrying the infection. IBD patients should be checked for Hepatitis B and immunized.

Hepatitis B

Hepatitis B is a virus that infects and replicates in the liver. It can be passed from mother to baby (vertical), through sexual contact, sharing needles and blood transfusions. Infection can result in liver cirrhosis (scarring of the liver) and liver cancer. However, the majority of patients who are chronically infected have no symptoms until very late in the disease process.

IBD patients should have their Hepatitis B immunity (titre) checked. The initiation of Anti-TNF medication (e.g. Humira, Remicade) can result in severe worsening of Hepatitis B infection in patients who are chronically infected.[5] For this reason, immunization is recommended in all non-immune patients.[2-4] Immunization involves two to three doses over a 6 month period.

Hepatitis A

Hepatitis A is a virus that infects and replicates within liver cells. It is transmitted primarily through things we eat (e.g. unsanitary food). It does not result in a chronic infection as the body is eventually able to clear it. A blood test can determine immunity from prior infection or immunization. Immunization involves two doses 6-12 months apart and a booster at 10 years.

Tdap

Tdap stands for tetanus, diphtheria and acellular pertussis. It is a killed (inactivated) combination, meaning it is safe to use even if one has a weakened immune system. Tetatnus and diphtheria (Td) should be administered every 10 years, and the accellular pertussis formulation (Tdap) should be administered at least once.[6]

Tetanus is caused by a neurotoxin produced by a bacterium that is found in the soil. Infection happens through a contaminated wound. It results in the involuntary contraction of muscles and can be fatal.

Diphtheria is a bacterial respiratory tract illness that can also involve the heart, skin and nerves. The decline of diphtheria closely mirrored the introduction of diphtheria immunization in the 1920s. It has largely been eliminated in Canada, with only a few cases reported per year. However, the possible consequence of stopping immunization for diseases that are thought to be eliminated was demonstrated in the former Soviet Union during the 1990s. Following years of declining immunization rates a diphtheria epidemic occurred with over 140000 cases and 4000 deaths reported.[6]

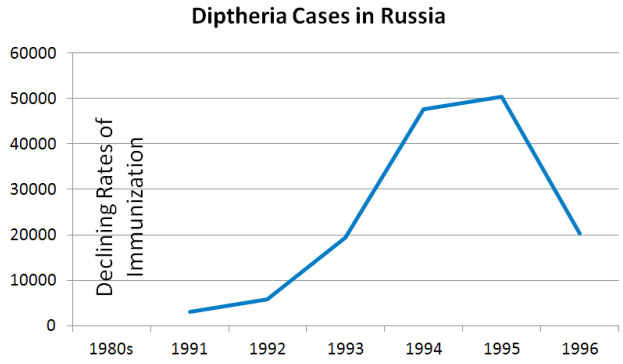

Fig 7: The danger in stopping immunizations for diseases no longer seen commonly was demonstrated in Russia during the 1990s. Declining immunization rates were followed by an outbreak of diphtheria.

Pertussis, or whooping cough, is caused by the respiratory bacterium *Bordetella pertussis*. A resurgence of pertussis occurred in Canada from 1990-2000 for a variety of reasons, but the incidence has dropped since the introduction of the acellular pertussis vaccine in the early 2000s.[6]

HPV

HPV, or the Human Papilloma Virus, infects the genital and oral (mouth) skin cells. It is usually spread through sexual contact and causes genital warts. This infection is particularly important in females as it can also cause cervical dysplasia, which can lead to cervical cancer. Females with IBD on immunosuppressant medication are at a 2 to 2.6 times increased risk of developing cervical dysplasia compared to the general population. Interestingly, even those on no medication – likely as a result of their disease being mild, had a higher risk than the general population.[7] This makes HPV vaccination in IBD patients especially important. Immunization is indicated in all females under the age of 26 and involves 3 doses given over 6 months.[2,3,6] Immunization may be considered in males and those over the age of 26.

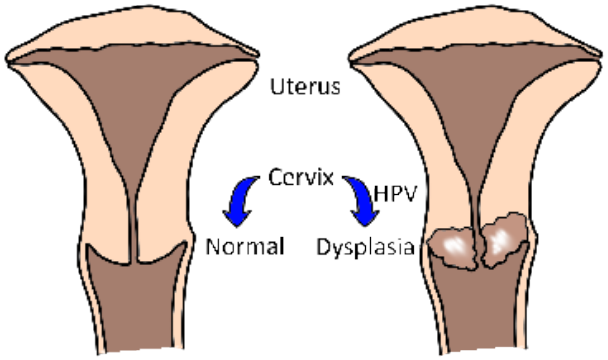

Fig 8: HPV infects and causes dysplasia of the cervix, which can lead to cancer. IBD patients are at higher risk of developing dysplasia, making immunization to prevent this process important.

Meningococcal

Neisseria Meningitidis is a bacteria transmitted from person-to-person through respiratory droplets. Some exposed individuals may develop invasive meningococcal disease (IMD), including meningitis (infection of the brain and its

lining). Immunization is indicated in patients with a non-functioning spleen, patients with HIV, military recruits and persons travelling to areas where infection is more common.[6] Immunization involves 2 doses given 8 weeks apart with a booster at 5 years.

MMR

MMR stands for measles, mumps and rubella. It is usually given as a childhood immunization (2 doses). Adults who do not have documented immunization can have a blood test to determine immunity. In non-immune patients with IBD, the vaccine may be given as long as the patient does not have a weakened immune system.[2] This restriction exists as the MMR vaccine is a live attenuated vaccine. It warrants mention that rubella infection during pregnancy is associated with the congenital rubella syndrome. This can result in deafness, eye abnormalities, congenital heart disease and intellectual disability. For this reason women of child-bearing age are a priority group that should ideally be immunized prior to pregnancy or starting immunosupressive medication.

Varicella Zoster Virus (Chicken Pox)

Varicella is the virus responsible for chicken pox. It is an airborne disease which can spread through coughing, sneezing or through direct contact with non-crusted skin lesions. Infection usually occurs in childhood. Based on case reports, an infection in someone without prior immunity (from having chicken-pox or the VZV immunization) who is simultaneously on anti-TNF therapy can be life-threatening.[5]

If a documented history of chicken pox or varicella immunization is not available, a blood test (titre) can be performed to determine one's immune status. If it is negative (non-immune), immunization is recommended and involves 2 doses at least 6 weeks apart. However, as it is a live attenuated vaccine, it cannot be given if someone has a weakened immune system.

Zoster (Shingles)

Zoster, more commonly referred to as shingles, is a condition also caused by the Varicella virus. After the initial infection with chicken-pox, the virus remains dormant in nerve cells and can reactivate later in life. This reactivation is referred to as shingles, and leads to a skin eruption in the distribution of the particular nerve it emerged from. Patients with IBD on immunosuppressant medication have a higher incidence of shingles (2.5-7 times) compared to the general population.[7] Patients with IBD mild enough to not require medication still have 1.6 times the risk of developing shingles.

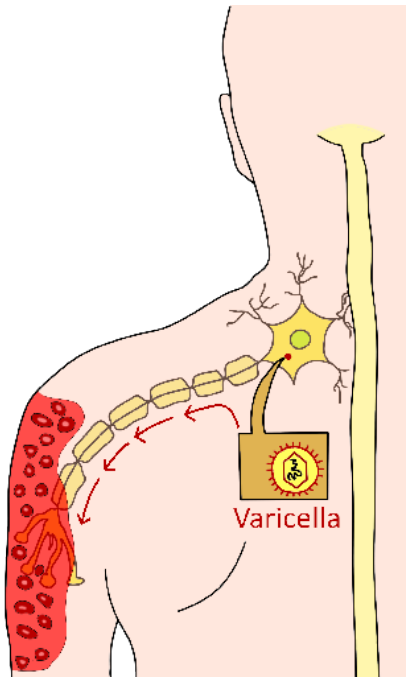

Fig 9: Varicella can reactivate in nerves and spread to cause skin lesions (Shingles). IBD patients are more prone to Shingles, but immunization can reduce this risk.

Immunization is meant to boost immunity in order to prevent re-activation of the virus, and is indicated in patients over the age of 60. It is given as a one-time dose. Again, as it is a live attenuated vaccine, it cannot be given if someone has a weakened immune system. No blood test (titre) is necessary prior to the zoster immunization.

When Is the Right Time To Get Immunizations?

The short answer to this question is as soon as possible. Immunization prior to any exposure to immunosuppressants may result in a better immune response. For example, the influenza, pneumococcal, tetanus and hepatitis B immunizations may not work quite as well with certain medication. The course of IBD can be hard to predict at times, and if a flare does occur, new medication may need to be started immediately. Some vaccines (live attenu-

ated) need to be withheld once someone is immunosupressed with medication, and so they may have missed the best opportunity to be immunized before the flare.

Will Immunization Cause an IBD Flare?

While isolated case reports of flares do exist, available data and expert opinion suggest immunizations will not cause an IBD flare. Likewise, data from other autoimmune diseases (such as Multiple Sclerosis, Rheumatoid Arthritis and Lupus) do not show worsening of disease as the result of immunizations. [2,3]

Adverse Reactions

On the whole immunizations are widely regarded as one of the greatest achievements of modern civilization. Many devastating diseases that were once commonplace, have now been eliminated. Immunizations are also generally very well tolerated. Mild symptoms may occasionally develop and these include[2]:

- Injection site reactions – tenderness/redness
- Occasionally fever and myalgias (sore muscles)
- Vaccine related rash with varicella/zoster immunization

For more in-depth immunization information and a thorough discussion of possible adverse reactions related to each individual vaccine please visit The Public Health Agency of Canada's Immunization Guide at:

- http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-eng.php [6]

Is There a Cost For Immunization?

The cost of some immunizations is publicly funded for residents of Nova Scotia. However, some immunizations may require a fee (Table 1), and one should check for coverage through extended medical benefits for these.

Where Can I Get Immunized?

The best way to arrange immunizations in Nova Scotia is through your general practitioner's office, through public health or through the NSCIBD and Hepatology clinic's special population vaccination clinic.

References

1. Lichtenstein GR, Feagan BG, Cohen RD, et al. Serious infection and mortality in patients with crohn's disease: More than 5 years of follow-up in the TREAT registry. Am J Gastroenterol. 2012;107(9):1409-1422.
2. Wasan SK, Baker SE, Skolnik PR, Farraye FA. A practical guide to vaccinating the inflammatory bowel disease patient. Am J Gastroenterol. 2010;105(6):1231-1238.
3. Rahier JF, Ben-Horin S, Chowers Y, et al. European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. J Crohns Colitis. 2009;3(2):47-91.
4. Allen J, Dassopoulos T. American gastroenterological association: Adult inflammatory bowel disease physician performance measures set. 2011:1-52.
5. Domm S, Cinatl J, Mrowietz U. The impact of treatment with tumour necrosis factor-alpha antagonists on the course of chronic viral infections: A review of the literature. Br J Dermatol. 2008;159(6):1217-1228.
6. Public Health Agency of Canada. Canadian immunization guide. http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-eng.php. Published 2012. Updated 2014. Accessed 01/29, 2014.
7. Marehbian J, Arrighi HM, Hass S, Tian H, Sandborn WJ. Adverse events associated with common therapy regimens for moderate-to-severe crohn's disease. Am J Gastroenterol. 2009;104(10):2524-2533.

Table 1: Immunization Recommendation Summary

Immunization	Type	Immuno-supressed	Indication	Schedule	Titre Check?	Cost*	Comment
Influenza	Inactivated	Can be given	All patients	Yearly	No	Funded	Live attenuated form (intra-nasal) contrain-dicated if immunosu-pressed
Pneumococcal	Inactivated	Can be given	All patients	Single dose & 5-year booster	No	Funded	
Hepatitis B	Inactivated	Can be given	All patients if negative titre	3 doses over 6 months	Yes	Variable	Check titre prior to immunization; check titre to ensure response
Hepatitis A	Inactivated	Can be given	All patients if negative titre	2 doses over 6 months	Yes	Not Funded	Check titre prior to immunization
Tdap	Inactivated	Can be given	All patients	Td every 10 years with one Tdap	No	Funded	
HPV	Inactivated	Can be given	Females < 26 yo	3 doses over 6 months	No	Variable	Greatest benefit for females given cervical cancer risk; May be considered in males and if age>26
Meningococcal	Inactivated	Can be given	Splenectomy, military re-cruits, travel	2 doses (8 weeks apart) and booster at 5 years	No	Not Funded	
MMR	Live attenuated	CONTRAin-dicated	Negative titre/ No childhood im-munization	2 doses (at least 4 weeks apart)	Yes	Variable	Should not initiate immunosupression for 6 weeks post immuni-zation
Varicella	Live attenuated	CONTRAin-dicated	Negative titre/ No childhood im-munization	2 doses (6 weeks apart)	Yes	Variable	Should not initiate immunosupression for 4-12 weeks post immunization
Zoster	Live attenuated	CONTRAin-dicated	Age > 60 & without con-traindication	1 dose	No	Not Funded	Should not initiate immunosupression for 4-12 weeks post immunization

*For immunizations that indicate 'variable' cost coverage, public funding will depend on a number of factors including age, medical conditions and type of work. More information can be obtained at the immunization assessment by Public Health.

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