VACCINE	USE IN PREGNANCY	USE IN BREASTFEEDING	COMMENTS
Yellow fever	**Generally contraindicated** unless travel to area at high risk of transmission is unavoidable and high level of mosquito protection is not feasible	**Generally contraindicated** unless travel to area at high risk of transmission is unavoidable and high level of mosquito protection is not feasible	• Seroconversion rates lower during pregnancy; post-immunization serology recommended • Limited data on fetal safety • Inadvertent immunization is not reason for pregnancy termination • Probable transmission of vaccine strain of yellow fever virus to the infant via breastfeeding has been reported

[1] when benefits outweigh risks

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PART 3

IMMUNIZATION OF INFANTS BORN PREMATURELY

BEST PRACTICES

Premature infants (defined as infants born before 37 weeks of gestational age) in stable clinical condition (regardless of birth weight) should be immunized with age-appropriate doses of vaccine at the same chronological age and according to the same schedule as full-term infants, with some exceptions as outlined below. Healthy premature infants generally tolerate immunizations well, with rates of adverse events similar to the low rates of full-term infants.

Passive transfer of maternal antibodies occurs after the 28th week of gestation. Therefore, premature infants born after 28 weeks of gestation will have maternally derived antibodies but at lower concentrations and for a shorter duration than full-term newborns. Premature infants of less than 28 weeks gestation are not expected to have significant amounts of maternal antibody. Thus, premature infants may experience increased frequency and severity of vaccine preventable illnesses and should be protected from vaccine preventable disease through timely immunization.

Antibody response to immunization is generally a function of chronological age. Some studies showed that premature infants seem to have lower antibody responses to vaccines than full-term infants. However, vaccine efficacy in premature infants remains high. Therefore, immunization of premature infants should not be delayed. Neonatal intensive care units and other hospital areas where premature infants may remain hospitalized for prolonged periods should have immunization programs in place.

Premature infants, especially those weighing less than 1,500 grams at birth are at higher risk of apnea and bradycardia following vaccination compared to full-term infants. Any increase or recurrence of apnea and bradycardia following vaccination of a premature infant is generally self-limited, subsides within 48 hours, and does not alter the infant's overall clinical progress. Hospitalized premature infants should have continuous cardiac and respiratory monitoring for 48 hours after their first immunization.

HEPATITIS B VACCINE

PREMATURE INFANTS OF MOTHERS WHO ARE HBSAG-NEGATIVE

The response to hepatitis B (HB) vaccine may be diminished in premature infants with birth weight less than 2,000 grams. In jurisdictions where the first dose is routinely given at birth, routine HB immunization of infants should be delayed until the infant reaches 2,000 grams or upon hospital discharge if discharge occurs before the infant has 2000 grams.

PREMATURE INFANTS OF MOTHERS WHO ARE HBSAG-POSITIVE

All premature infants, regardless of weight, born to women who are HBsAg-positive should receive HB immune globulin (HBIg) and monovalent HB vaccine within 12 hours of birth.

Premature infants weighing **2,000 grams or more** at birth should receive three doses of HB vaccine, given at birth, 1 and 6 months of age. Monovalent HB vaccine should be given for the doses at birth and 1 month; DTaP-HB-IPV-Hib vaccine can be used for the 6-month dose. Premature infants weighing **less than 2,000 grams** at birth should receive four doses of HB vaccine, given at birth, 1, 2 and 6 months of age. The final dose in the vaccine series should not be administered before 24 weeks of age. Monovalent HB vaccine should be given for the doses at birth and 1 month; DTaP-HB-IPV-Hib vaccine can be used for the 2 and 6-month doses.

All premature infants of HBsAg-positive mothers should have an assessment of the anti-HBs titre 4 weeks after their series of HB vaccine has been completed to assess the success of immunoprophylaxis. If HBsAg is present, the child will likely become a chronic hepatitis B carrier. If the infant is negative for both HBsAg and anti-HBs (i.e., a non-responder), additional doses of HB vaccine (up to a second full course) should be given with repeated serologic testing for antibody response.

PREMATURE INFANTS OF MOTHERS WITH UNKNOWN HBSAG STATUS

If maternal HBsAg status is not available within 12 hours of delivery, consideration should be given to administering HB vaccine and HBIg to the infant while the results are pending, *taking into account the mother's risk factors* and erring on the side of providing vaccine and HBIg if there is any suspicion that the mother could be infected.

Refer to Hepatitis B Vaccine in Part 4 for additional information.

PNEUMOCOCCAL VACCINE

Prematurity is associated with an increased risk of chronic lung disease. Children with chronic lung disease are at increased risk of invasive pneumococcal disease. A 4-dose conjugate pneumococcal vaccine schedule (at 2, 4, 6 and 15 to 18 months of age) is recommended for premature infants with chronic lung disease or other conditions resulting in high risk of invasive pneumococcal disease. The first dose of conjugate pneumococcal vaccine should be given at 2 months of age, even if the infant is still hospitalized. Refer to Pneumococcal Vaccine in Part 4 for additional information.

ROTAVIRUS VACCINE

Available data indicate that rotavirus vaccine is safe and effective in preterm infants. Given the potential complications of rotavirus infections in premature infants and the benefits of vaccination, rotavirus vaccines are recommended for premature infants starting at 6 weeks of chronological age, with the first dose administered no later than 14 weeks of chronological age. Rotavirus vaccine may be considered for hospitalized infants, after discussion with infection control services and neonatologists. The vaccination series should be completed by 8 months of chronological age. Refer to Rotavirus Vaccine in Part 4 for additional information.

MONOCLONAL ANTI-RESPIRATORY SYNCYTIAL VIRUS (RSV) ANTIBODY (PALIVIZUMAB)

To decrease the likelihood of serious RSV infection requiring hospitalization and supplemental oxygen therapy, palivizumab (SYNAGIS®, Abbott Laboratories Ltd.) should be recommended for:

- all infants born prematurely at 32 weeks gestation or earlier who are 6 months of chronological age or younger at the start of the RSV season
- selected infants born prematurely between 32 and 35 weeks gestational age who are less than 6 months of age at the start of the RSV season
- selected infants and children 24 months of age and younger with chronic lung disease or hemodynamically significant congenital heart disease

Refer to *Palivizumab* in *Passive Immunizing Agents* in Part 5 for additional information and definition of selected infants.

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PART 3

IMMUNIZATION OF PATIENTS IN HEALTH CARE INSTITUTIONS

In both acute and long term health care settings, it is important that immunization efforts be part of organized care plans within each department, with clear accountability for program planning, implementation and evaluation. There is good evidence that the use of health care provider reminders and standing orders or medical directives, as well as evaluation of vaccine coverage with feedback to health care providers improves vaccine uptake. Immunization programs or increased uptake of available vaccines has been associated with decreased antibiotic usage. Antibiotic usage reductions ranged from 5% to 10% in randomized controlled trials to relative reductions of 64% in observational studies.

Recommended vaccination schedules differ among the provinces and territories; therefore, immunization schedule differences may need to be considered when discharging a patient to another jurisdiction. When transferring a patient, information about the patient's immunization status should be provided to the receiving institution.

ACUTE CARE INSTITUTIONS

Admission to hospital as well as visits to outpatient clinics or the emergency department provide important opportunities for health care providers to evaluate immunization status and offer vaccination to patients of all ages. For patients without regular sources of health care or those followed in specialized clinics, the only opportunities for immunization may be during clinic visits or hospitalization.

Special considerations are needed when administering live vaccines in a hospital setting. In addition to routine practices, further infection control precautions may be indicated when giving rotavirus vaccine or live attenuated influenza virus (LAIV) vaccine in the hospital setting. For example, if a rash occurs following vaccination with a varicella-containing vaccine, the rash may need to be covered. There may be some viral shedding following rotavirus vaccination; this could pose a risk if there was potential contact with a severely immunocompromised patient. Consultation with the hospital's Infection Control experts is advised. Live vaccines are generally not administered to immunocompromised patients; refer to *Immunization of Immunocompromised Persons* in Part 3 for information about vaccination of immunocompromised people.

Protocols for reporting adverse events following immunization should be in place in acute care institutions. Patients may be admitted to hospital for a serious adverse event following immunization. In addition, patients who receive a vaccine in hospital may experience an adverse event. Any adverse event following immunization that results in hospital admission or prolongs hospitalization is considered a serious adverse event and needs to be reported. Refer to *Vaccine Safety* in Part 2 for additional information about reporting adverse events following immunization.

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PREGNANT WOMEN

The immunization status of any pregnant woman admitted to hospital should be assessed and arrangements made to optimize her immunization status. Offering inactivated influenza vaccine during pregnancy is particularly important as pregnant women are at increased risk of serious illness, complications, and hospitalization from influenza infection. Influenza vaccination during pregnancy also protects the newborn infant from infection. Pregnant women who have not previously received Tdap vaccine in adulthood should be vaccinated immediately post-partum. During an outbreak, the use of tetanus-reduced diphtheria-reduced acellular pertussis (Tdap) vaccine in pregnancy may be considered in the second half of pregnancy for those not previously vaccinated in adulthood. Pertussis vaccine in pregnancy is currently under National Advisory Committee on Immunization (NACI) review. Live vaccines are generally contraindicated during pregnancy; if live vaccines, such as rubella-containing vacines, are needed, plans should be put in place to provide the vaccines post-partum. Refer to *Immunization in Pregnancy and Breastfeeding* in Part 3 for additional information.

NEWBORNS AND INFANTS

Newborns of hepatitis B infected women should receive post-exposure prophylaxis (hepatitis B vaccine and hepatitis B immune globulin) within 12 hours of birth. As well, administration of the first dose of hepatitis B vaccine to other newborns at high risk of exposure to hepatitis B virus may be considered before discharge. Refer to *Hepatitis B Vaccine* in Part 4 for additional information.

Neonatal intensive care units (NICU) should have immunization programs in place for infants who remain in the NICU for two months or longer. In general, premature infants should receive routine vaccines according to their chronologic age. Refer to *Immunization in Pregnancy and Breastfeeding* and *Immunization of Infants Born Prematurely* in Part 3 for additional information.

In areas of high tuberculosis rates and lack of access to detection and treatment services, BCG vaccine may be indicated. Refer to *Bacille Calmette-Guerin (BCG) Vaccine* in Part 4 for additional information.

POST-PARTUM WOMEN AND OTHER CLOSE CONTACTS OF NEWBORNS

Women susceptible to rubella and/or varicella should receive vaccine post-partum before discharge. Arrangements should be made for varicella-susceptible women to receive a second dose of univalent varicella vaccine at least 6 weeks after the first dose. Women who did not receive influenza vaccination during pregnancy should receive influenza vaccine before discharge if it is influenza season. Arrangements should be made for household and other close contacts to receive influenza vaccine, and for parents (as well other adults who anticipate having regular contact with an infant) who have not previously received acellular pertussis-containing vaccine in adulthood, to receive a dose of Tdap vaccine as soon as possible. Adolescents who anticipate having regular contact with a newborn should receive Tdap vaccine if they have not already received an adolescent booster dose. Refer to *Pertussis vaccine* in Part 4 and *Immunization in Pregnancy and Breastfeeding* in Part 3 for additional information.

CHILDREN AND ADOLESCENTS

Hospitalization may be an ideal opportunity to ensure catch up of routine childhood immunizations. Recommendations may need to be modified depending on the underlying condition leading to hospitalization. Refer to *Immunization of Immunocompromised Persons* in Part 3 for additional information regarding children and adolescents who may be hospitalized with immunodeficiency disorders, or undergoing chemotherapy for malignant hematologic disorders. Refer to *Immunization of Persons with Chronic Diseases* in Part 3 for additional information about hospitalized children and adolescents who have chronic conditions.

ADULTS

There is an increasing number of vaccines recommended for adults (refer to *Immunization of Adults* in Part 3 for additional information). Despite the growing list of recommended adult immunizations, young and middle-aged adults (especially men) tend to have fewer contacts with the health care system than

either children or the elderly; therefore, opportunistic immunization of adults during hospitalization is very important.

Many immunosuppressive or chronic disorders are associated with increased susceptibility to complications of vaccine-preventable diseases in adults. Refer to *Immunization of Immunocompromised Persons* in Part 3 for additional information on adults who may be hospitalized with HIV or other immunodeficiency disorders. Refer to *Immunization of Persons with Chronic Diseases* in Part 3 for additional information on hospitalized adults who have chronic conditions. .

THE ELDERLY

The admission of elderly patients to hospital is an opportunity to optimize their immunization status. Effective programs to vaccinate elderly patients before discharge or while attending a clinic will guarantee that they do not miss influenza immunization in the community during the limited influenza vaccination period. It is also a useful time to assess whether a tetanus and diphtheria toxoid-containing (Td) vaccine booster dose or Tdap vaccine is needed. Zoster and pneumococcal vaccine should also be considered. Refer to *Immunization of Persons with Chronic Diseases* in Part 3 for additional information on those with cardiac, renal, hepatic, metabolic and endocrine or pulmonary conditions.

LONG TERM CARE INSTITUTIONS

Residents of long term care facilities, including children, should receive all routine immunizations, as appropriate for their age and risk status. The following vaccines are particularly important to consider: Herpes zoster (in those 60 years of age and older), pneumococcal, and influenza. Td vaccine is recommended every 10 years for adults, and this may be an opportunity to also provide polio or pertussis vaccine in the previously unimmunized or under-immunized population.

Annual seasonal influenza immunization is essential for nursing home or chronic and continuing care facility residents of any age. Programs and strategies should be implemented to ensure that annual influenza immunization occurs. Residents in long term care facilities that have standing order programs for influenza are more likely to be immunized. Patients and/or their surrogate decision makers should be advised of the facility's immunization policy on admission and every effort made to obtain informed consent before the influenza season.

Refer to *Immunization of Immunocompromised Persons* and *Immunization of Persons with Chronic Diseases* in Part 3 for additional information on immunization recommendations for residents with specific disorders.

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PART 3

IMMUNIZATION OF PERSONS WITH CHRONIC DISEASES

Chronic diseases may increase a person's risk of infection and/or increase a person's risk of more severe disease should infection occur. There is also an increased risk of nosocomial exposure to vaccine preventable diseases due the increased likelihood of prolonged hospitalization and frequent outpatient visits associated with chronic disease. Therefore, it is important that people with chronic diseases who are immunocompetent be immunized with both live and inactivated vaccines according to routine immunization schedules. Vaccines may be less immunogenic in this population and additional vaccines, additional doses, or higher dosages of vaccines may be required to provide adequate protection. Ideally, vaccination is best accomplished early in the disease when the response is likely to be similar to other persons of a similar age with no chronic medical condition. If a disease progresses and immunosuppressive therapy is required, vaccine requirements and recommendations may change. Refer to Table 1 for a summary of recommendations for vaccination of persons with chronic diseases. Refer to Immunization of Immunocompromised Persons in Part 3 for information about vaccination of people who are immunosuppressed.

ASPLENIA OR HYPOSPLENIA

Asplenic or hyposplenic people have absent or defective splenic function. This can occur as a result of congenital absence of the spleen, surgical removal of the spleen, or medical conditions that result in poor or absent splenic function (e.g., sickle cell disease, thalassemia major). All people, regardless of age, who have absent or defective splenic function are at increased risk of fulminant bacteremia which is associated with a high mortality rate. Risk is highest in the first two years following splenectomy but remains elevated for life.

Careful attention should be paid to immunization status when "elective" surgical splenectomy is planned so that all of the necessary vaccines are administered at least 2 weeks before surgery. In the case of an emergency splenectomy, vaccines are best given 2 weeks after the splenectomy for optimal vaccine responses. If the person is discharged earlier and there is a concern that he/she might not return, vaccines should be given before discharge.

There are no contraindications to the use of any vaccine for people known to be asplenic or hyposplenic. Such persons should receive all routine vaccinations. Particular attention should be paid to ensuring that asplenic or hyposplenic individuals of all ages receive *Haemophilus influenzae* type b (Hib), meningococcal and pneumococcal vaccines according to recommended schedules, as these individuals are highly susceptible to encapsulated bacteria. Influenza vaccine is recommended annually. Hepatitis A and Hepatitis B vaccines are indicated for those who require repeat transfusions (e.g., sickle cell anemia). For children, some routine vaccinations, such as varicella vaccine, are given on a different schedule than the routine age-based recommendation.

HAEMOPHILUS INFLUENZAE TYPE B (HIB) VACCINE

All people with asplenia or hyposplenia should receive Hib vaccine:

- Children (less than 5 years of age) should receive an age appropriate primary series of Hib vaccine.
- People 5 years of age and older, including adults, should receive a single dose of Hib vaccine, regardless of previous Hib immunization, and at least 1 year after any previous dose.

Refer to *Haemophilus influenzae type b Vaccine* in Part 4 for additional information.

HEPATITIS A AND HEPATITIS B VACCINES

People with sickle cell anemia that results in functional asplenia may require repeat transfusions. People receiving repeated transfusions of blood or blood products are considered to be at higher risk of contracting hepatitis A and hepatitis B and should be offered hepatitis A and hepatitis B vaccines.

INFLUENZA VACCINE

Asplenic or hyposplenic people should receive yearly influenza vaccine as appropriate for age. Influenza vaccination lowers the risk of secondary bacterial infections. For children with chronic health conditions, there is insufficient evidence to recommend live attenuated influenza vaccine (LAIV) preferentially over trivalent inactivated influenza vaccines (TIV). For adults with chronic health conditions, there is insufficient evidence to recommend the use of LAIV, particularly given the evidence suggesting better immune response to TIV in this age group. Refer to *Influenza Vaccine* in Part 4 for additional information.

MENINGOCOCCAL VACCINE

All people with asplenia or hyposplenism should receive quadrivalent conjugate meningococcal vaccine (Men-C-ACYW-135). The schedule for those who are previously unimmunized is as follows:

- Children aged 2 to 11 months should receive 2 or 3 doses of Menveo™ given 8 weeks apart (with another dose given between 12 to 23 months of age and at least 8 weeks from the previous dose) and booster doses as outlined below.
- Children aged 12 to 23 months should receive 2 doses of Menveo™ vaccine given at least 8 weeks apart and booster doses as outlined below.
- People aged 2 to 55 years should receive 2 doses of a Men-C-ACYW-135 vaccine (either Menactra® or Menveo™) 8 weeks apart and booster doses as outlined below.
- Adults aged 56 years and over should receive 2 doses of a Men-C-ACYW-135 vaccine (either Menactra® or Menveo™) 8 weeks apart and booster doses as outlined below. Men-C-ACYW-135 vaccines are not authorized for use in people 56 years of age and over; however, based on limited evidence and expert opinion, Men-C-ACYW-135 vaccine use is considered appropriate.

If only one dose of Men-C-ACYW-135 vaccine was previously given, give another dose at the earliest opportunity and proceed with booster doses as outlined below based on the interval from the second dose.

A booster dose of Men-C-ACYW-135 vaccine should be given every 3 to 5 years for those last vaccinated at 6 years of age and younger, and every 5 years after the last dose for those last vaccinated at 7 years

of age and older. There is no role for meningococcal polysaccharide vaccine. Refer to *Meningococcal Vaccine* in Part 4 for additional information.

PNEUMOCOCCAL VACCINE

Infants and children

Asplenic or hyposplenic infants should receive a primary series of 4 doses of pneumococcal conjugate 13-valent vaccine (Pneu-C-13) given at age 2, 4, 6, and 12 to 15 months of age. Children between 12 and less than 24 months of age should get 2 doses of Pneu-C-13 vaccine, at least 8 weeks apart. Children (24 months of age and older) need only one dose of Pneu-C-13 vaccine. Even if a child received all recommended doses of Pneu-C-7 or Pneu-C-10 vaccine in the past, they should be given Pneu-C-13 vaccine as soon as possible.

Pneu-C-13 vaccine primes the immune system and should be followed by the broader spectrum, though less immunogenic, pneumococcal polysaccharide 23-valent vaccine (Pneu-P-23) for supplemental protection. One dose of Pneu-P-23 vaccine should be given at or after 24 months of age and at least 8 weeks after all doses of Pneu-C-13 vaccine required for age have been given. A single re-immunization with Pneu-P-23 after 5 years is recommended in persons who were 11 years of age or over at the time of initial immunization with Pneu-P-23 vaccine. A single re-immunization with Pneu-P-23 after 3 years is recommended for those who were 10 years of age or younger at the time of initial immunization with Pneu-P-23 vaccine. No more than two lifetime doses of Pneu-P-23 vaccine (initial dose and booster dose) are recommended.

Adults

For adults with asplenia or hyposplenia, one dose of Pneu-C-13 vaccine followed at least 2 months later by one dose of Pneu-P-23 vaccine is recommended. One lifetime booster dose of Pneu-P-23 vaccine is recommended 5 years after the initial dose of Pneu-P-23 vaccine.

Refer to *Pneumococcal Vaccine* in Part 4 for additional information.

VARICELLA VACCINE

Susceptible hyposplenic or asplenic individuals should receive two doses of univalent varicella vaccine, at least 3 months apart (instead of 6 weeks apart as routinely recommended for adolescents and adults). Refer to *Varicella (Chickenpox) Vaccine* in Part 4 for additional information.

CHRONIC RENAL DISEASE/DIALYSIS

Bacterial and viral infections are a major cause of morbidity and mortality in people with renal disease or who are undergoing chronic dialysis (hemodialysis or peritoneal dialysis). People with chronic renal disease and dialysis may have mild defects in T cell function and may experience a less than optimal response to vaccine. In people with nephrotic syndrome, urinary loss of antibody may occur. These persons are also in frequent contact with the health care system and may be exposed to respiratory diseases. They are at greater risk for complications from respiratory viruses and pneumococcal disease. Rare transmissions of viral hepatitis B and/or C may also occur.

In addition to routine immunization, hepatitis B, influenza and pneumococcal vaccines are recommended in people with chronic renal disease or who are undergoing dialysis. Refer to *Immunization of Immunocompromised Persons* in Part 3 for additional information about renal transplant candidates and recipients.

HEPATITIS B VACCINE

There is a poor response to hepatitis B vaccine in people with chronic renal disease or who are undergoing dialysis and the antibody to hepatitis B surface antigen (anti-HBs) concentration declines

rapidly. Therefore, immunization with a higher dosage of hepatitis B vaccine (e.g., 40 micrograms for adult) is recommended. Post-immunization serologic testing within 1 to 6 months of completion of the vaccine series is recommended with re-immunization with a second series if anti-HBs antibody titres are less than 10 IU/L. For those who respond to the vaccine, the anti-HBs concentration should be evaluated yearly and booster doses (using a higher vaccine dosage) should be given as necessary. Refer to *Hepatitis B Vaccine* in Part 4 for additional information.

INFLUENZA VACCINE

In general, immunogenicity of influenza vaccine is reduced in persons with chronic renal disease. For children with chronic health conditions, there is insufficient evidence to recommend LAIV preferentially over TIV. For adults with chronic health conditions, there is insufficient evidence to recommend the use of LAIV, particularly given the evidence suggesting better immune response to TIV in this age group. Refer to *Influenza Vaccine* in Part 4 for additional information.

PNEUMOCOCCAL VACCINE

Children with chronic renal disease should receive Pneu-C-13 vaccine followed by Pneu-P-23 vaccine at 2 years of age or older. Adults should receive Pneu-P-23 vaccine. One lifetime re-immunization with Pneu-P-23 vaccine is recommended. Refer to *Pneumococcal Vaccine* in Part 4 for additional information.

VARICELLA VACCINE

Susceptible individuals over 12 months of age with chronic renal disease or who are undergoing dialysis should receive two doses of univalent varicella vaccine at least 3 months apart (instead of 6 weeks apart as routinely recommended for adolescents and adults). Refer to *Varicella (Chickenpox) Vaccine* in Part 4 for additional information on dosing intervals according to age.

NEUROLOGIC DISORDERS

Neurologic disorders appear at different ages and, therefore, will affect immunization decisions. Disorders that usually begin during infancy, such as cerebral palsy, spina bifida, seizure disorder, neuromuscular diseases and inborn errors of metabolism, may have symptom onset before the receipt of the vaccines routinely recommended in infancy. Other conditions, such as autism spectrum disorders, acute demyelinating encephalomyelitis, Guillain-Barré syndrome (GBS), transverse myelitis and multiple sclerosis are known to be diagnosed in childhood and adulthood over the same time period as routine vaccines are administered and may occur before or after the administration of vaccines.

People with pre-existing neurological disorders should receive all routinely recommended immunizations without delay (with the exception of repeat doses of any vaccine given within 6 weeks of the onset of an episode of GBS). Adults who have a history of myelitis or fibromyalgia should be reassured that routine immunization is recommended for its protective effects and poses no concern with respect to their condition. In addition to routine immunization, people with neurological conditions that compromise the management of respiratory secretions and are associated with an increased risk of aspiration should receive influenza vaccine; those with chronic cerebrospinal fluid (CSF) leak or neurologic conditions that may impair clearance of oral secretions should receive pneumococcal vaccines.

INFLUENZA VACCINE

Adults and children 6 months of age and older with neurological conditions that compromise the management of respiratory secretions and are associated with an increased risk of aspiration should receive yearly influenza vaccination. For children with chronic health conditions, there is insufficient evidence to recommend LAIV preferentially over TIV. For adults with chronic health conditions, there is insufficient evidence to recommend the use of LAIV, particularly given the evidence suggesting better immune response to TIV in this age group. Refer to *Influenza Vaccine* in Part 4 for additional information.

PNEUMOCOCCAL VACCINE

People with chronic CSF leak or chronic neurologic conditions that may impair clearance of oral

secretions and place them at risk of aspiration should receive pneumococcal vaccines. Children with these conditions should receive Pneu-C-13 vaccine followed by Pneu-P-23 vaccine at 2 years of age or older. Adults should receive Pneu-P-23 vaccine. Refer to *Pneumococcal Vaccine* in Part 4 for additional information.

CHRONIC LUNG DISEASE

Individuals with chronic lung diseases such as asthma, chronic obstructive pulmonary diseases (COPD), or cystic fibrosis are at increased risk of complications of influenza and pneumococcal infection. Those with cystic fibrosis are also at increased risk of complications from varicella infection. In more severe chronic lung disease, many of these persons may have bacterial colonization due to poor mucociliary clearance and bronchiectasis and defects in pulmonary macrophage function. Smoking also impairs mucociliary clearance and predisposes to pneumococcal disease. In addition to routine immunization, people with chronic lung disease should receive influenza and pneumococcal vaccines. Additionally, those with cystic fibrosis should receive varicella vaccine.

INFLUENZA VACCINE

Adults and children with chronic lung disorders (including bronchopulmonary dysplasia, cystic fibrosis and asthma) should receive seasonal influenza vaccine yearly. Individuals with severe asthma (defined as currently on high dose inhaled or oral glucocorticosteroids, or active wheezing) should receive TIV, as LAIV should not be administered to individuals with severe asthma or those with medically attended wheezing in the 7 days prior to vaccination. For children with chronic health conditions, there is insufficient evidence to recommend LAIV preferentially over TIV. For adults with chronic health conditions, there is insufficient evidence to recommend the use of LAIV, particularly given the evidence suggesting better immune response to TIV in this age group. Refer to *Influenza Vaccine* in Part 4 for additional information.

PNEUMOCOCCAL VACCINE

People with chronic pulmonary disease (including adults with asthma requiring regular medical care) and adult smokers should receive pneumococcal vaccine. Children with chronic lung diseases should receive Pneu-C-13 vaccine followed by Pneu-P-23 vaccine at 2 years of age or older. Adults should receive Pneu-P-23 vaccine. Refer to *Pneumococcal Vaccine* in Part 4 for additional information.

VARICELLA VACCINE

Susceptible people with cystic fibrosis are a priority for varicella immunization because varicella disease may cause a transient worsening of lung function. Refer to *Varicella (Chickenpox) Vaccine* in Part 4 for additional information.

Refer to *Immunization of Immunocompromised Persons* in Part 3 for additional information about vaccination of lung transplant candidates and recipients.

CHRONIC HEART DISEASE

Persons with chronic heart disease have mild defects in T cell function. Viral and bacterial infections may precipitate cardiac decompensation and lead to hospitalization. In addition to routine immunization, people with cardiac disorders should receive influenza vaccine annually. Those with chronic heart disease should receive pneumococcal vaccines.

INFLUENZA VACCINE

People with congenital heart disease, coronary artery disease, and congestive heart failure are at high risk of influenza-related complications and should receive seasonal influenza vaccine annually. There are some data to suggest that those with congestive heart failure may have a weaker response to the influenza vaccine and are, therefore, at higher risk particularly when exposed to new influenza strains. There is evidence that giving influenza vaccine to those with coronary artery disease has some protective

effect on subsequent cardiac events. For children with chronic health conditions, there is insufficient evidence to recommend LAIV preferentially over TIV. For adults with chronic health conditions, there is insufficient evidence to recommend the use of LAIV, particularly given the evidence suggesting better immune response to TIV in this age group. Refer to *Influenza Vaccine* in Part 4 for additional information.

PNEUMOCOCCAL VACCINE

People with heart disease are at increased risk of invasive pneumococcal disease and should receive pneumococcal vaccines. Children with cardiac disease should receive Pneu-C-13 vaccine followed by Pneu-P-23 vaccine at 2 years of age or older. Adults should receive Pneu-P-23 vaccine. Refer to *Pneumococcal Vaccine* in Part 4 for additional information.

CHRONIC LIVER DISEASE

Persons with chronic liver disease have impaired phagocyte function and defects in opsonizing antibody. They may also have splenic dysfunction if the liver disease is severe. Hepatic encephalopathy or chronic alcohol consumption may lead to aspiration pneumonia. Alcoholism is also a risk factor for invasive pneumococcal disease. Newly acquired hepatitis A or hepatitis B in persons who already have chronic liver disease from another cause could lead to rapid hepatic decompensation. Those with ascites have an altered immunoglobulin production and distribution. People with HIV who are on antiretroviral therapy may also have liver disease.

In addition to routine immunization, people with chronic liver disease should receive influenza, pneumococcal, hepatitis A, and hepatitis B vaccines. Vaccination should be completed early in the course of liver disease for optimal immunogenicity.

HEPATITIS A VACCINE

Hepatitis A vaccine is recommended for non-immune persons with chronic liver disease, including those infected with hepatitis B or C, because they are at risk of more severe disease if infection occurs. Vaccination should be completed early in the course of the disease, as the immune response to vaccine is suboptimal in advanced liver disease. Refer to *Hepatitis A Vaccine* in Part 4 for additional information.

HEPATITIS B VACCINE

Hepatitis B vaccine is recommended for non-immune persons with chronic liver disease, including those infected with hepatitis C, because they are at risk of more severe disease if infection occurs. Vaccination should be completed early in the course of the disease, as the immune response to vaccine is suboptimal in advanced liver disease. Anti-HBs titre testing may be used to document hepatitis B vaccine response. For people with advanced liver disease, including disease caused by hepatitis C, seroconversion should be assessed after hepatitis B vaccination and consideration given to revaccinating with a higher dose hepatitis B vaccine for those who are did not respond to the first series (i.e., who do not achieve an anti-HBs titre of at least 10 IU/L). Refer to *Hepatitis B Vaccine* in Part 4 for additional information.

PNEUMOCOCCAL VACCINE

People with chronic liver disease (including hepatic cirrhosis due to any cause) or alcoholism are at increased risk of invasive pneumococcal disease and should receive pneumococcal vaccines. Children with chronic liver disease should receive Pneu-C-13 vaccine followed by Pneu-P-23 vaccine at 2 years of age or older. Adults should receive Pneu-P-23 vaccine. One lifetime re-immunization with Pneu-P-23 vaccine is recommended. Refer to *Pneumococcal Vaccine* in Part 4 for additional information.

Refer to *Immunization of Immunocompromised Persons* in Part 3 for additional information about vaccination of hepatic transplant candidates and recipients, and HIV-infected people.

ENDOCRINE AND METABOLIC DISEASES

Routine immunization is recommended for persons with endocrine and metabolic disorders. It is generally

not expected that vaccines would interfere with insulin levels or glucose control. People with diabetes mellitus, however, have defects in phagocytic and neutrophil function. In addition, they often have complications of diabetes such cardiovascular, neurovascular, renal and other end-organ dysfunction. They are also at greater risk of complications from infection, such as influenza. In addition to routine immunization, people with diabetes should receive influenza and pneumococcal vaccines. Persons with morbid obesity (Body Mass Index of 40 or higher) are also at high risk of influenza-related complications and annual influenza vaccine is recommended.

HEPATITIS B VACCINE

The National Advisory Committee on Immunization (NACI) is reviewing evidence related to the use of hepatitis B vaccine for adults with diabetes mellitus (type 1 and type 2).

INFLUENZA VACCINE

Influenza immunization reduces hospitalization and deaths in persons with diabetes mellitus and is recommended annually. Vaccination is also recommended for individuals with other metabolic diseases, such as thyroid disorders. For children with chronic health conditions, there is insufficient evidence to recommend LAIV preferentially over TIV. For adults with chronic health conditions, there is insufficient evidence to recommend the use of LAIV, particularly given the evidence suggesting better immune response to TIV in this age group. Refer to *Influenza Vaccine* in Part 4 for additional information.

PNEUMOCOCCAL VACCINE

People with diabetes should also receive pneumococcal vaccines. Diabetic children should receive Pneu-C-13 vaccine followed by Pneu-P-23 vaccine at 2 years of age or older. Adults should receive Pneu-P-23 vaccine. Refer to *Pneumococcal Vaccine* in Part 4 for additional information.

NON-MALIGNANT HEMATOLOGIC DISORDERS

Non-malignant hematologic disorders include anemias and hemoglobinopathies, as well as bleeding disorders. For further discussion on vaccines recommended for people with anemia due to sickle cell disease, refer to *Asplenia or hyposplenia*.

ANEMIAS, HEMOGLOBINOPATHIES

People with anemia may be at increased risk of complications from vaccine preventable diseases; routine immunization is recommended. People with anemias or hemoglobinopathies should receive influenza vaccine annually, pneumococcal vaccines and if there is a need for repeat transfusions, hepatitis A and hepatitis B vaccines.

Influenza vaccine

People with anemias or hemoglobinopathies are at high risk of influenza-related complications and should receive influenza vaccine annually. For children with chronic health conditions, there is insufficient evidence to recommend LAIV preferentially over TIV. For adults with chronic health conditions, there is insufficient evidence to recommend the use of LAIV, particularly given the evidence suggesting better immune response to TIV in this age group. Refer to *Influenza Vaccine* in Part 4 for additional information.

Pneumococcal vaccine

People with hemoglobinopathies are at increased risk of invasive pneumococcal disease and should receive pneumococcal vaccines. Children with hemoglobinopathies, should receive Pneu-C-13 vaccine followed by Pneu-P-23 vaccine. One lifetime re-immunization with Pneu-P-23 vaccine is recommended. Refer to *Pneumococcal Vaccine* in Part 4 for additional information.

Hepatitis A hepatitis B vaccine

People with hemoglobinopathies, such as some thalessemias, who are receiving repeated infusions of blood or blood products are considered to be at higher risk of contracting hepatitis A and hepatitis B and should be offered hepatitis A and hepatitis B vaccines.

BLEEDING DISORDERS

People with bleeding disorders may differ from the normal population with respect to the risk of hematoma formation from intramuscular (IM) injections and the potentially increased risk of infection as a result of their disease and exposure to blood products. Before beginning immunization of any child, vaccine providers should ensure that there are no symptoms or signs compatible with an undiagnosed bleeding disorder. If such indicators are present, a diagnosis should be established before commencing immunization. For example, in any male child who has a history of an intramuscular hematoma following an intramuscular injection, an undiagnosed bleeding disorder, such as hemophilia, should be considered. If a disorder is present, it should be optimally managed prior to immunization to minimize the risk of bleeding.

Hepatitis A vaccine

Hemophiliacs and people receiving repeated infusions of blood or blood products are considered to be at higher risk of contracting hepatitis A and should be offered hepatitis A vaccine. If hepatitis B vaccine is also indicated, both vaccines can be given as a combination vaccine.

Hepatitis B vaccine

Hemophiliacs and people receiving repeated infusions of blood or blood products are considered considered for pre-immunization testing if they have had repeated exposure to blood products. In an unvaccinated individual with a bleeding disorder in whom passive immunization with hepatitis B immune globulin (HBIg) may be indicated due to an exposure, it is recommended to give clotting factor concentrates prior to giving HBIg. Refer to *Hepatitis B Vaccine* in Part 4 for additional information.

Vaccine administration

For people with bleeding disorders, special measures need to be considered before administering vaccine. Any bleeding disorder should be optimally controlled. For example, hemophiliacs may receive clotting factor concentrates to optimize their clotting factor level before they receive a parenteral vaccine.

Generally there is no evidence of increased risk of bleeding in those with bleeding disorders following IM versus subcutaneous injections. There is some evidence to suggest that IM administration may generally be safe when given with a small gauge needle (23 gauge or smaller) and firm pressure is applied to the injection site for 5-10 minutes. One study assessing immunization by the subcutaneous route for vaccine intended for intramuscular administration identified this was associated with more local reactogenicity and a diminished immune response compared to the IM route.

ANTICOAGULATION

Individuals receiving long-term anticoagulation with either warfarin or heparin are not considered to be at higher risk of bleeding complications following immunization and may be safely immunized through either the IM or subcutaneous route as recommended without discontinuation of their anticoagulation therapy. Two studies of immunization of people on anticoagulant therapy showed no significant increase in bleeding complications with the IM route. There is a paucity of evidence on whether there is an increased risk of bleeding complications following immunization with the newer types of anticoagulants, such as antiplatelet agents.

CHRONIC INFLAMMATORY DISEASES

This population includes persons with inflammatory arthropathies (e.g., systemic lupus erythematosus [SLE], rheumatoid or juvenile arthritis etc.), inflammatory dermatologic conditions, and inflammatory bowel disease (Crohn's disease, ulcerative colitis). Infections are one of the most common causes of morbidity,

hospitalization and death in people with SLE. People with inflammatory arthritis are also at increased risk of vaccine preventable infections. This risk is thought to be due to both an altered immune response associated with the autoimmune condition itself and to the immunosuppressive nature of the treatments required to control the underlying inflammatory condition. Respiratory tract infections are the most common infectious cause of hospital consultation in immunosuppressed people with rheumatic diseases. Influenza and *Streptococcus pneumonia* infections are common. At least one study has shown that children with rheumatic disease have lower antibody concentrations and seroprotection rates than healthy controls against mumps, rubella, diphtheria and tetanus (but not measles). Inflammatory bowel disease rates have increased globally over the past few years and there appears to be some alteration of immune receptors and an increased risk of opportunistic infections with inflammatory bowel disease, including vaccine preventable diseases, such as influenza.

CHRONIC INFLAMMATORY DISEASES NOT TREATED WITH IMMUNOSUPPRESSIVE DRUGS

Individuals with autoimmune disease **not being treated with immunosuppressive drugs** are not considered significantly immunocompromised and can receive routine immunization including live vaccines following consultation with their physician. The nature of the person's underlying disease and treatment should be considered. Rheumatic disease modifying agents such as hydroxychloroquine, sulfasalazine, or auranofin are not generally identified as immunosuppressive. Refer to *Immunization of Immunocompromised Persons* in Part 3 for a list of immunosuppressive medications.

CHRONIC INFLAMMATORY DISEASES TREATED WITH IMMUNOSUPPRESSIVE THERAPIES

Monoclonal antibody therapy

Monoclonal antibodies (MAB) – which may be called anti-TNF agents or biologics – are biological drugs that may be used to treat inflammatory bowel disease, rheumatoid arthritis, psoriatic arthritis and spondyloarthropathies as well as some dermatologic conditions, such as psoriasis. Common MAB include infliximab and adalimumab. MAB can be used singly or in combination with other immunosuppressive therapies.

Recommended immunization prior to monoclonal antibody therapy

The immunization status of people anticipated to receive MAB should be optimized prior to initiation of therapy due to their increased risk of opportunistic infections. Vaccination with Pneu-P-23 vaccine is recommended and hepatitis B vaccination may be considered in seronegative patients. Annual influenza vaccination with TIV is indicated. Varicella vaccination (if varicella susceptible) or herpes zoster vaccination may be considered.

Immunization while monoclonal antibody therapy is ongoing

The safety and efficacy of live vaccines during treatment with MABs is unknown. There have been reported cases of reactivation of latent tuberculosis infection and predisposition to other opportunistic infections. Therefore, until additional information becomes available, avoidance of live vaccines during MAB therapy is prudent. Annual influenza vaccine with TIV is indicated for people receiving MAB. Refer to *Immunization of Immunocompromised Persons* in Part 3 for additional information about vaccination of people receiving MAB and other immunosuppressive therapies.

Monoclonal antibodies taken during pregnancy will be transferred to the fetus and their effects may persist after birth. Refer to *Immunization in Pregnancy and Breastfeeding* in Part 3 for additional information.

OTHER CONDITIONS

CANCER

People with cancer have a higher risk of contracting infectious diseases and a higher risk of developing complications likely because many cancers and their treatments affect the immune system. Therefore, it is important that children and adults with cancer receive protection from vaccine preventable diseases

whenever possible. Generally, cancer alone is not sufficient to make someone immunocompromised such that he/she cannot receive live vaccines. Because chemotherapy may lead to an immunocompromised state, immunization should be completed before beginning chemotherapy if possible.

Recommended vaccines will depend on the type of cancer and the type of treatment. For hematologic cancers or for people on immunosuppressive therapies, refer to *Immunization of Immunocompromised Persons* in Part 3. For patients with cancer treated with monoclonal antibodies, refer to *Monoclonal Antibody Therapy*. It is important to assess and optimize the vaccination status of anyone close to people with cancer to reduce the risk of exposure to vaccine preventable diseases. Refer to *Close Contacts* for additional information.

DERMATOLOGIC DISORDERS

Inflammatory dermatologic disorders may include psoriasis, severe atopic dermatitis and eczema. Treatment is generally topical anti-inflammatories. Vaccines should be given as per the routine schedule. Care should be taken to not administer vaccine into affected areas, as this may exacerbate the condition.

CHRONIC SALICYLATE THERAPY IN CHILDREN LESS THAN 18 YEARS OF AGE

Individuals receiving low doses of salicylate therapy (e.g., acetylsalicylic acid [e.g., aspirin, ASA]) are not considered to be at increased risk of bleeding complications following immunization. However, for children and adolescents on chronic salicylate therapy, special consideration must be given when administering live influenza and varicella vaccines as outlined below.

Influenza vaccine

Children and adolescents with conditions treated for long periods with ASA are at high risk of influenza-related complications and should receive influenza vaccine annually. Live attenuated influenza vaccine (LAIV) should not be administered to children currently receiving ASA because of the theoretical risk of Reye's syndrome with ASA and wild-type influenza infection. Reye's syndrome, which causes damage to the brain and liver, is a rare complication that most commonly occurs in children taking ASA who develop a viral infection. ASA-containing products should be delayed for four weeks after receipt of LAIV in children less than 18 years of age. Refer to *Influenza Vaccine* in Part 4 for additional information.

Varicella vaccine

Varicella-susceptible children and adolescents receiving chronic salicylate therapy (e.g., ASA) are a priority for varicella immunization because of an association between wild-type varicella disease, salicylate therapy and the risk of Reye's syndrome. Varicella-containing vaccine manufacturers recommend avoidance of salicylate therapy for 6 weeks after varicella immunization because of an association between wild-type varicella, salicylate therapy and Reye's syndrome. Health care providers should weigh the theoretical risks associated with varicella vaccine against the known risks associated with wild-type varicella infection. Because adverse events have not been reported with the use of salicylates after varicella immunization, people with conditions requiring chronic salicylate therapy should be considered for immunization, with close subsequent monitoring. Refer to *Varicella (Chickenpox) Vaccine* in Part 4 for additional information.

COCHLEAR IMPLANTS

Children who have received a cochlear implant are at increased risk for meningitis from some pathogens and otitis media. People with cochlear implants or those who are receiving cochlear implants should receive all age appropriate vaccinations, including Pneu-C-13, Hib, and influenza vaccines. Children 24 months and older should also receive a single dose of Pneu-P-23 vaccine.

CO-MORBIDITIES

Guidance on immunization for those with more than one chronic condition is an emerging area of inquiry; evidence to inform guidance on immunization of people with co-morbidities is lacking. There is some evidence that co-morbidities may have additive risk for complications from vaccine-preventable diseases, such as influenza. As a general principle, when considering immunization of people with co-morbidities, all conditions and medications should be considered in relation to the indications, precautions and contraindications for each vaccine.

CLOSE CONTACTS

Up-to-date routine immunizations, including annual influenza vaccine, are recommended for household members and other close contacts, including health care workers, of people with chronic diseases. Refer to *Immunization of Workers* and *Immunization of Immunocompromised Persons* in Part 3 for additional information.

Table 1: Vaccination of persons with chronic diseases
(Refer to text and vaccine-specific chapters in Part 4 for additional information)

Vaccine	Chronic disease								
	Asplenia/ hyposplenia	Renal diseases/ dialysis	Neurologic disorders	Lung disease	Liver disease	Endocrine/ metabolic diseases	Heart disease	Chronic inflammatory diseases	Non-malignant hematologic disorders
Inactivated vaccines									
Cholera and travellers' diarrhea	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated
Diphtheria	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use
Haemophilus influenzae type b (Hib)	Recommended for all ages	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use
Hepatitis A	Use if indicated[2]	Use if indicated	Use if indicated	Use if indicated	Recommended	Use if indicated	Use if indicated	Use if indicated	Recommended for hemophiliacs and people receiving repeated infusions of blood or blood products
Hepatitis B	Routine use[2]	Recommended	Routine use	Routine use	Recommended	Routine use	Routine use	Routine use	Recommended for hemophiliacs and people receiving repeated infusions of blood or blood products
HPV	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use
Influenza (TIV)	Recommended annually	Recommended annually	Recommended annually	Recommended annually	Routine use	Recommended annually	Recommended annually	Recommended annually if immune suppressed	Recommended annually for people with anemias or hemoglobinopathies
Japanese encephalitis	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated

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Vaccine	Chronic disease								
	Asplenia/ hyposplenia	Renal diseases/ dialysis	Neurologic disorders	Lung disease	Liver disease	Endocrine/ metabolic diseases	Heart disease	Chronic inflammatory diseases	Non-malignant hematologic disorders
Meningococcal quadrivalent conjugate	Recommended for all ages	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use
Pertussis	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use
Pneumococcal conjugate 13-valent	Recommended for all ages	Children recommended	Children recommended	Children recommended	Children recommended	Children recommended	Children recommended	Recommended in immunosuppressed	Children and adults with hemoglobinopathies recommended
Pneumococcal polysaccharide 23-valent	Recommended for children 2 years of age and older and adults[9]	Recommended for children 2 years of age and older and adults[9]	Recommended for children 2 years of age and older and adults	Recommended for children 2 years of age and older and adults[9]	Recommended for children 2 years of age and older and adults[9]	Recommended for those with diabetes	Recommended for children 2 years of age and older and adults	Recommended in immunosuppressed	Recommended for children 2 years of age and older and adults with hemoglobinopathies
Polio (inactivated)	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use
Rabies	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated
Tetanus	Routine use	Routine use	Routine use[10]	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use
Typhoid (inactivated)	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated
Live vaccines									
BCG	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated if no immune suppression	Use if indicated

Vaccine	Chronic disease								
	Asplenia/ hyposplenia	Renal diseases/ dialysis	Neurologic disorders	Lung disease	Liver disease	Endocrine /metabolic diseases	Heart disease	Chronic inflammatory diseases	Non-malignant hematologic disorders
Herpes zoster	Use if indicated	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Use if indicated if no immune suppression	Routine use
Influenza (LAIV)	TIV preferred[11]	TIV preferred[11]	TIV preferred[11]	TIV preferred[11]	TIV preferred[11]	TIV preferred[11]	TIV preferred[11]	TIV preferred[11]	TIV preferred[11]
Measles-mumps-rubella	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use if no immune suppression	Routine use
Rotavirus	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use	Routine use if no immune suppression	Routine use
Smallpox	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Contraindicated in non-outbreak situation	Contraindicated in non-outbreak situation for people with dermatologic conditions	Use if indicated
Typhoid (live)	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated if no immune suppression	Use if indicated
Varicella (univalent)	Routine use[12]	Routine use[12]	Routine use	Routine use[13]	Routine use	Routine use	Routine use	Use if indicated if no immune suppression	Routine use
Yellow fever	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated	Use if indicated if no immune suppression	Use if indicated

1. Consider optimizing control of bleeding disorders prior to receipt of parenteral vaccine. Note: For people with sickle cell disease, refer to Asplenia section.
2. Vaccine recommended for conditions requiring repeated transfusions (e.g., sickle cell disease).
3. Higher dosage recommended; post-immunization serology recommended with re-immunization if hepatitis B surface antigen (anti-HBs) less than 10 IU/L; periodic monitoring of anti-HBs titre recommended.

4. Vaccinate early in course of hepatic disease; post-immunization serology may be used; for people with advanced liver disease, assess seroconversion and consider re-immunization with increased antigen content vaccine if anti-HBs less than 10 IU/L.
5. For people with neurologic conditions that compromise the management of respiratory secretions and are associated with an increased risk of aspiration.
6. Except people known to have developed GBS within 6 weeks of previously receiving an influenza vaccine.
7. Periodic re-immunization with meningococcal quadrivalent conjugate vaccine also recommended. Refer to *Meningococcal Vaccine* in Part 4.
8. One lifetime re-immunization with Pneu-P-23 vaccine also recommended.
9. For people with chronic CSF leak or chronic neurologic conditions that may impair clearance of oral secretions.
10. Except people known to have developed GBS within 6 weeks of previously receiving a tetanus-toxoid containing vaccine.
11. LAIV can be used in children with chronic conditions, but not preferentially. TIV is recommended for adults with chronic conditions. LAIV is contraindicated for persons with severe asthma or active wheezing – use TIV.
12. Two doses of varicella vaccine should be given 3 months apart.
13. Susceptible people with cystic fibrosis are a priority for varicella immunization.
14. There is an association between yellow fever vaccine-associated viscerotropic disease and a history of thymus disease; therefore, yellow fever vaccine is not generally recommended for persons with a history of thymoma, thymectomy or myasthenia gravis.

TIV = trivalent inactivated influenza vaccine
LAIV = live attenuated influenza vaccine

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PART 3

IMMUNIZATION OF IMMUNOCOMPROMISED PERSONS

GENERAL RECOMMENDATIONS AND PRINCIPLES

The safety and effectiveness of vaccines in immunocompromised persons are determined by the type of immunodeficiency and degree of immunosuppression. Each immunocompromised person is different and presents unique considerations regarding immunization. The relative degree of immunodeficiency is variable depending on the underlying condition. Immunodeficiency can also vary over time in many people and the decision to recommend for or against a particular vaccine will depend upon a case-by-case analysis of the risks and benefits. There is potential for serious illness and death if immunocompromised people are under-immunized and every effort should be made to ensure adequate protection through immunization; however, inappropriate use of live vaccines can cause serious adverse events in some immunocompromised people as a result of uncontrolled replication of the vaccine virus or bacterium.

The following recommendations reflect general best practices and are subject to individual considerations and new evidence as it arises.

INACTIVATED VACCINES

Inactivated vaccines may be administered to immunocompromised people if indicated because the antigens in the vaccine cannot replicate and there is no increase in the risk of vaccine-associated adverse events; however, the magnitude and duration of vaccine-induced immunity are often reduced. When considering immunization of an immunocompromised person with an inactivated vaccine, consultation with the individual's attending physician may be of assistance in addition to the guidance provided in this chapter and in the Part 4 vaccine-specific chapters of the Canadian Immunization Guide. For complex cases, referral to a physician with expertise in immunization and/or immunodeficiency is advised.

LIVE VACCINES

In general, **immunocompromised people should not receive live vaccines because of the risk of disease caused by the vaccine strains**. People who are severely immunocompromised or in whom immune status is uncertain should not receive live vaccines. In less severely immunocompromised people, the benefits of vaccination with routinely recommended live vaccines may outweigh risks. When considering immunization of an immunocompromised person with a live vaccine, **approval from the individual's attending physician should be obtained before vaccination**. In complex cases, referral to a physician with expertise in immunization and/or immunodeficiency is advised.

SEROLOGIC TESTING AND RE-IMMUNIZATION

Immune response to vaccines may be inadequate in immunocompromised people and vaccines may remain susceptible despite appropriate vaccination. If serologic testing is available and there is a clear antibody correlate of protection, measurement of post-immunization antibody titres to determine immune

response and guide re-vaccination and post-exposure management should be considered. Refer to vaccine-specific chapters in Part 4 for additional information.

GENERAL PRINCIPLES

Several general principles apply to the immunization of immunocompromised individuals:

- Maximize benefit while minimizing harm.
- Susceptibility or degree of protection vary according to degree of immune suppression.
  - In a severely immunosuppressed person, such as someone who has had a hematopoietic stem cell transplant, there may not be complete protection even when there is a history of childhood infection or previous immunization.
- Immunize at the time when maximum immune response can be anticipated.
  - Immunize early before immunodeficiency begins, if possible.
  - Delay immunization if the immunodeficiency is transient (if this can be done safely).
  - Stop or reduce immunosuppression to permit better vaccine response, if appropriate.
- Consider the immunization environment broadly.
  - Vaccinate close contacts when appropriate.
  - Strongly encourage up-to-date vaccinations, including annual influenza vaccination, for all healthcare workers providing care to immunocompromised people.
- Avoid live vaccines unless:
  - immunosuppression is mild and data are available to support their use.
  - the risk of natural infection is greater than the risk of immunization.
- Monitor vaccinees carefully and boost aggressively.
  - The magnitude and duration of vaccine-induced immunity are often reduced in immunocompromised individuals.

FAMILY OR MEDICAL HISTORY

Immunodeficiency states may be undiagnosed in young children presenting for routine immunizations, which include live vaccines. This is particularly important to consider in infants receiving live vaccines **before 12 months of age.**

Clues pointing to the presence of significant immunodeficiency may be found in the medical or family history. Children with a history of failure to thrive and/or recurrent serious infections such as pneumonia or sepsis may have an immunodeficiency. A family history of congenital immunodeficiency may be known or may be suspected on the basis of a family history of early infant deaths. However, many congenital immunodeficiencies are autosomal recessive so the family history can be negative. Maternal HIV infection puts the infant at risk of immunodeficiency in the first year of life. Routine prenatal blood work in Canada includes HIV testing. A history of negative prenatal screening of the infant's mother for HIV should be obtained before administering a live vaccine to an infant less than 12 months of age. If a mother has not received routine prenatal care in Canada, the possibility of undiagnosed HIV infection should be considered.

CONGENITAL (PRIMARY) IMMUNODEFICIENCY

Congenital immunodeficiency states are generally inherited and include defects in antibody production (e.g., agammaglobulinemia, isotype and IgG subclass deficiencies, common variable immunodeficiency), complement deficiencies, defects in one or more aspects of cell-mediated immunity, and mixed deficits. Individuals with defects in antibody and complement are highly susceptible to encapsulated bacteria such as *Streptococcus pneumoniae*, *Haemophilus influenza* type b (Hib) and *Neisseria meningitidis*. Individuals with mixed and T cell defects are particularly susceptible to virtually all viruses and some bacteria.

As a general rule, people with antibody defects can be protected from many of the vaccine preventable infections with the use of replacement immune globulin (Ig) or pathogen-specific Ig preparations; however, the level of antibody to specific pathogens may be variable and vaccination is recommended to

increase the level of protection. Receipt of replacement Ig is not a contraindication for vaccination; however, Ig can interfere with the immune response to some live attenuated viral vaccines such as measles and varicella vaccine. Refer to *Blood Products, Human Immune Globulin and Timing of Immunization* in Part 1 for the recommended intervals between Ig and subsequent immunization.

Refer to *Immunization of Persons with Chronic Diseases* in Part 3 for information regarding immunization of asplenic or hyposplenic people.

INACTIVATED VACCINES

Inactivated vaccines should be administered to people with congenital immunodeficiency states according to routine immunization schedules. All individuals with congenital immunodeficiency disorders should receive pneumococcal, hepatitis B and Hib vaccines; annual immunization with trivalent inactivated influenza vaccine is recommended. In addition, persons with complement, properdin, factor D or primary antibody deficiencies should be vaccinated with quadrivalent conjugate meningococcal vaccine. Refer to *Table 1* and vaccine-specific chapters in Part 4 for additional information.

LIVE VACCINES

All live vaccines are contraindicated for people with T cell, natural killer T cell, and mixed cellular and antibody defects (e.g. Severe Combined Immune Deficiency [SCID]). Inadvertent live vaccine administration and exposure to natural infections can be managed with rapid administration of Ig or pathogen-specific Ig with or without appropriate antiviral or antibacterial treatment.

In general, live vaccines are not recommended for individuals with other congenital immunodeficiency states, with the following exceptions:

- People with **X-linked agammaglobulinemia and Common Variable Immunodeficiency (and known intact T cell immunity)** generally should not receive live vaccines. However, they should be considered for measles-mumps-rubella (MMR), and univalent varicella vaccines as appropriate for age. Regular immune globulin replacement therapy may affect the efficacy of these live vaccines. All other live vaccines such as rotavirus, Bacille Calmette-Guérin (BCG) and oral typhoid are contraindicated.

- People with **isolated IgA deficiency who have no concomitant defects in T cell function** can receive most live vaccines. Live mucosal vaccines (rotavirus, live attenuated influenza vaccine [LAIV], oral typhoid) are likely safe and may be used although there may be lack of mucosal response; some experts may prefer to use inactivated vaccines (e.g., inactivated trivalent influenza vaccine, parenteral inactivated typhoid vaccine). However, given that there are limited data on the use of live mucosal vaccines, consultation with an immunologist is advised and immunization with these vaccines should be individually assessed.
  - People with **IgG subclass deficiencies** can receive live vaccines although response may be suboptimal. In addition, regular immune globulin replacement therapy may diminish response to a live vaccine.

- People with **phagocytic and neutrophil disorders** (e.g., congenital neutropenia, leukocyte adhesion and migration defects, chronic granulomatous disease) may be vaccinated with MMR, rotavirus, univalent varicella, herpes zoster, LAIV, or yellow fever vaccine, if indicated. Live bacterial vaccines (BCG and oral typhoid vaccine) are contraindicated.
- People with **complement deficiency** (e.g., properdin or factor D deficiency) may receive any live vaccine, if indicated.

Refer to Table 1 and Table 2 for recommendations for vaccination of persons with congenital immunodeficiency and vaccine-specific chapters in Part 4 for additional information.

Table 1: Vaccination of persons with congenital immunodeficiency – inactivated vaccines
(Refer to text and vaccine-specific chapters in Part 4 for additional information)

Inactivated vaccine	Congenital immunodeficiency				Comments
	B cell deficiency	T cell, mixed defects	Phagocytic & neutrophil disorders	Complement deficiency	
Cholera and travellers' diarrhea (inactivated)	Use if indicated	Use if indicated	Use if indicated	Use if indicated	
Diphtheria	Routine use[1]	Routine use	Routine use	Routine use	
***Haemophilus influenzae* type b (Hib)**	Children less than 5 years of age: routine use	Children less than 5 years of age: routine use	Children less than 5 years of age: routine use	Children less than 5 years of age: routine use	• Refer to Haemophilus influenzae type B Vaccine in Part 4 for additional information
	Individuals 5 years of age and older: 1 dose recommended[2]	Individuals 5 years of age and older: 1 dose recommended[2]	Individuals 5 years of age and older: 1 dose recommended[2]	Individuals 5 years of age and older: 1 dose recommended[2]	
Hepatitis A	Use if indicated	Use if indicated	Use if indicated	Use if indicated	• Pre-exposure prophylaxis for travel: consider Ig with hepatitis A vaccine • Post-exposure prophylaxis: Ig recommended along with vaccine • Refer to Hepatitis A Vaccine in Part 4 for additional information
Hepatitis B	Recommended	Recommended	Recommended	Recommended	• Higher dosage recommended • Post-immunization serology testing of anti-HBs titres recommended with re-immunization if response less than 10 IU/L • Periodic monitoring of anti-HBs titre recommended • Refer to Hepatitis B Vaccine in Part 4 for additional information

Inactivated vaccine	Congenital Immunodeficiency				Comments
	B cell deficiency	T cell, mixed defects	Phagocytic & neutrophil disorders	Complement deficiency	
HPV	Routine use	Routine use	Routine use	Routine use	○ 3-dose schedule recommended
Influenza (inactivated)	Recommended	Recommended	Recommended	Recommended	• Recommended annually • Refer to Influenza Vaccine in Part 4 for additional information
Japanese encephalitis	Use if indicated	Use if indicated	Use if indicated	Use if indicated	
Meningococcal conjugate	Quadrivalent conjugate meningococcal vaccine recommended	Quadrivalent conjugate meningococcal vaccine recommended	Routine use	Quadrivalent conjugate meningococcal vaccine recommended	• Refer to Meningococcal Vaccine in Part 4 for additional information
Pertussis	Routine use	Routine use	Routine use	Routine use	
Pneumococcal conjugate 13-valent (Pneu-C-13)	Recommended	Recommended	Recommended	Recommended	• Fair evidence to recommend • Refer to Pneumococcal Vaccine in Part 4 for additional information • Should be followed – at least 2 months later or when reaches age 2 years – with a pneumococcal polysaccharide vaccine dose
Pneumococcal polysaccharide (Pneu-P-23)	Recommended	Recommended	Recommended	Recommended	• One life-time re-immunization recommended • Refer to Pneumococcal Vaccine in Part 4 for additional information
Polio (inactivated)	Routine use	Routine use	Routine use	Routine use	

Inactivated vaccine	Congenital immunodeficiency				Comments
	B cell deficiency	T cell, mixed defects	Phagocytic & neutrophil disorders	Complement deficiency	
Rabies	Use if indicated	Use if indicated	Use if indicated	Use if indicated	• Do not use intradermally • Post-immunization serology recommended • Refer to Rabies Vaccine in Part 4 for additional information
Tetanus	Routine use	Routine use	Routine use	Routine use	
Typhoid (inactivated)	Use if indicated	Use if indicated	Use if indicated	Use if indicated	

[1] routine use: follow routine immunization schedules with age-appropriate booster doses
[2] regardless of prior history of Hib vaccination and at least 1 year after any previous dose

anti-HBs: antibody to hepatitis B surface antigen
Ig: immune globulin

Table 2: Vaccination of persons with congenital immunodeficiencies – live attenuated vaccines
(Refer to text and vaccine-specific chapters in Part 4 for additional information)

Live attenuated vaccine	Congenital immunodeficiency					Comments
	B cell deficiency		T cell, mixed defects	Phagocytic & neutrophil disorders	Complement deficiency	
	X-linked agammaglobulinemia & Common Variable Immunodeficiency	IgA deficiency & IgG subclass deficiency				
BCG	Contraindicated	Use if indicated	Contraindicated	Contraindicated	Use if indicated	
Herpes zoster	Contraindicated	Routine use[1]	Contraindicated	Routine use	Routine use	
Influenza (live)	Contraindicated – use inactivated	Consider use[2, 3]	Contraindicated – use inactivated	May receive if indicated	May receive if indicated	• Refer to Influenza Vaccine in Part 4 for additional information
Measles-mumps-rubella	Consider use[4]	Routine use[4]	Contraindicated	Routine use	Routine use	• Complement deficiency: consider post-immunization serology and re-immunization, if protective titres not achieved • Refer to Measles Vaccine in Part 4 for additional information
Rotavirus	Contraindicated[3]	Consider use[2]	Contraindicated	Routine use	Routine use	
Smallpox	Contraindicated	Use if indicated	Contraindicated	Use if indicated	Use if indicated	
Typhoid (live)	Contraindicated; if indicated, use inactivated	Consider use[2,3]	Contraindicated; if indicated, use inactivated	Contraindicated; if indicated, use inactivated	Use if indicated	

Live attenuated vaccine	Congenital immunodeficiency					
	B cell deficiency		T cell, mixed defects	Phagocytic & neutrophil disorders	Complement deficiency	Comments
	X-linked agammaglobulinemia & Common Variable Immunodeficiency	IgA deficiency & IgG subclass deficiency				
Varicella (univalent)	Consider use[4]	Routine use[4]	Contraindicated	May be given 2 doses at least 3 months apart	May be given 2 doses at least 3 months apart	• Consider post-immunization serology • Refer to Varicella (Chickenpox) Vaccine in Part 4 for additional information
Yellow fever	Contraindicated	Use if indicated	Contraindicated	Use if indicated	Use if indicated	

1 routine use: follow routine immunization schedules with age-appropriate booster doses
2 consult with immunologist in cases of IgA deficiency
3 some experts may prefer inactivated vaccine for persons with IgA deficiency
4 regular immune globulin replacement therapy may affect the efficacy of the vaccine. Refer to Blood Products, Human Immune Globulin and Timing of Immunization in Part 1 for the recommended intervals between Ig and subsequent immunization.

Ig: immune globulin

ACQUIRED (SECONDARY) IMMUNODEFICIENCY

Acquired immunodeficiency states result from diseases or infection that directly or indirectly cause immunosuppression (e.g., malignant hematologic disorders or solid tumours, hematopoietic stem cell transplantation, solid organ transplantation, HIV-infection) or long-term immunosuppressive therapy (e.g., long-term steroids, cancer chemotherapy, radiation therapy) used for organ transplantation and a range of chronic infectious and inflammatory conditions (e.g., inflammatory bowel disease, psoriasis, systemic lupus erythematosis). Refer to Immunization of Persons with Chronic Diseases in Part 3 for information regarding immunization of asplenic or hyposplenic people.

ACQUIRED COMPLEMENT DEFICIENCY

People with conditions such as paroxysmal nocturnal hemoglobinuria who are receiving the terminal complement inhibitor eculizumab (Soliris™, Alexion Pharmaceuticals Inc.) should receive two doses of quadrivalent conjugate meningococcal vaccine. They must be vaccinated at least two weeks prior to receiving the first dose of eculizumab, if possible, and every 5 years thereafter if they continue to use the drug.

MALIGNANT HEMATOLOGIC DISORDERS

(e.g., leukemia, lymphomas or other malignant neoplasms affecting the bone marrow or lymphatic systems)

Inactivated vaccines

Inactivated vaccines should be administered to people with malignant hematologic disorders according to routine immunization schedules. Individuals with malignant neoplasms, including lymphoma and leukemia, should receive pneumococcal and Hib vaccines because of increased susceptibility to disease. Annual immunization with trivalent inactivated influenza vaccine is also recommended.

Live vaccines

Live vaccines are contraindicated in individuals with severe immunodeficiency due to blood dyscrasias, lymphomas, leukemias of any type, or other malignant neoplasms affecting the bone marrow or lymphatic systems and in people undergoing immunosuppressive treatment for malignancy.

Children with Acute Lymphocytic Leukemia (ALL) may be vaccinated with MMR vaccine with or without varicella vaccine if the disease has been in remission for at least 12 months, the child's total lymphocyte count is at least 1.2×10^9/L, the child is not receiving radiation therapy, and maintenance chemotherapy can be withheld for at least 1 week before to 1 week after immunization. Refer to Varicella (Chickenpox) Vaccine in Part 4 for additional information. Persons with leukemia in remission and who have not received immunosuppressive chemotherapy or radiation for at least 3 months and who do not have defects in T cell function can receive herpes zoster vaccine if indicated. Refer to Herpes Zoster (Shingles) Vaccine in Part 4 for additional information.

MALIGNANT SOLID TUMOURS

Inactivated vaccines

Inactivated vaccines should be administered to people with malignant solid tumours according to routine immunization schedules. In addition, pneumococcal vaccines should be given because of increased susceptibility to invasive pneumococcal disease. Annual immunization with trivalent inactivated influenza vaccine is also recommended.

Live vaccines

Live vaccines are contraindicated in people undergoing immunosuppressive treatment for any malignant solid tumours. In general, if a patient is 3 months post-chemotherapy and the cancer is in remission, the person is no longer considered immunocompromised.

HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT – autologous or allogeneic)

HSCT is the transplantation of blood-derived or bone marrow-derived hematopoietic stem cells following bone marrow ablation or non-ablative conditioning by chemotherapy or radiation. HSCT recipients receive either their own cells (autologous HSCT) or cells from a donor (allogeneic HSCT). Cells are sourced from bone marrow, peripheral blood, or umbilical cord blood.

Antibody titres to vaccine-preventable diseases decrease after allogeneic or autologous HSCT if the HSCT recipient is not revaccinated post-transplant. Virtually all HSCT recipients experience a prolonged period of immune suppression following transplantation. Allogeneic HSCT recipients experience profound immune suppression in the early post-transplant period but relatively normal immunity after 1 to 2 years if they are off immunosuppressive medication and free of graft-versus-host disease (GVHD). GVHD generally does not occur.

Immunity after transplant must be at least partially reconstituted for a vaccine to mount a clinically significant response. In general, T cells capable of responding to new antigens are generated at 6 to 12 months after transplant, earlier in young children and later in adults. The differences in responses of autologous and allogeneic HSCT recipients to vaccines are not well characterized and approaches to vaccination are the same. Efficacy data for vaccines in HSCT recipients are limited.

Vaccination in accordance with transplant centre-specific immunization guidelines is generally part of routine post-transplant care provided by many transplant centers.

Pre-HSCT

If time permits, careful consideration must be given to the pre-ablation immunization status of the HSCT candidate. If the transplant is planned during the influenza season, trivalent inactivated influenza vaccine should be given at least 2 weeks prior to transplant. People awaiting HSCT should not receive live vaccines. Donor vaccination may improve responses of the HSCT recipient to some vaccines; however, in general, due to logistical and ethical issues, donor vaccination is not practiced.

Post-HSCT

HSCT recipients should be viewed as "never immunized" and require re-immunization after transplant because the ablation of hematopoietic cells in the bone marrow pre-transplant eliminates the person's immune memory. In addition, certain vaccine preventable diseases pose increased risk for HSCT recipients of all ages (e.g., pneumococcal, *Haemophilus influenzae* type b, measles, varicella, and influenza). Quadrivalent conjugate meningococcal vaccine should be given if indicated by age and risk factors for invasive meningococcal disease. HSCT recipients respond poorly to polysaccharide vaccines, such as pneumococcal polysaccharide 23-valent vaccine. If serologic testing is available and there is a clear antibody correlate of protection, measurement of post-immunization antibody titres to determine immune response and guide re-vaccination and post-exposure management should be considered.

Inactivated vaccines

Inactivated vaccines should be repeated for HSCT recipients generally beginning 6 to 12 months post-transplant (pneumococcal conjugate vaccine may be given beginning at 3 to 9 months post-transplant, trivalent inactivated influenza vaccine may be given beginning at 4 to 6 months post-transplant). Refer to *Table 3* and vaccine-specific chapters in Part 4 for recommendations for HSCT recipients.

Live vaccines

MMR and univalent varicella vaccines may be considered 24 months or more post-transplant for HSCT recipients provided there is no evidence of chronic GVHD, immunosuppression has been discontinued for at least 3 months, and the person is considered immunocompetent by a transplant specialist. Refer to Table 3 and vaccine-specific chapters in Part 4 for recommendations for HSCT recipients.