ALTERED IMMUNOCOMPETENCE

Layout of Altered Immunocompetence

- General Principles
- Altered Immunocompetence as an Indication to Receive a Vaccine
- Vaccination of Contacts of Persons with Altered Immunocompetence
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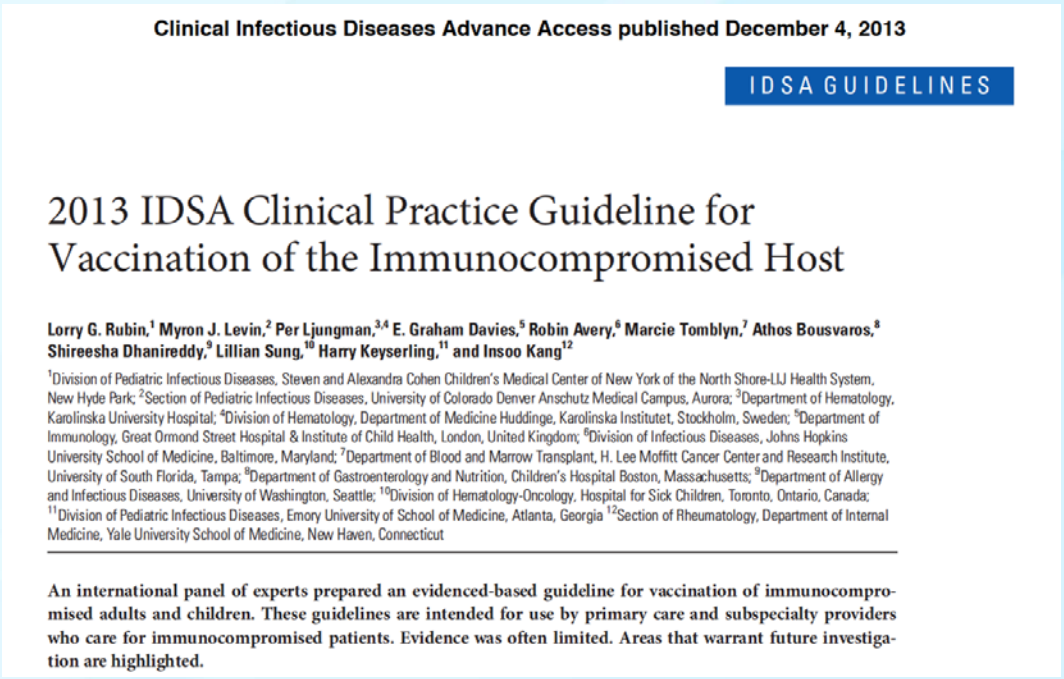
- Recipients of Hematopoietic Cell Transplants (HCT)
- Conditions or Drugs that Might Cause Immunodeficiencies

General Recommendations – Altered Immunocompetence

- New guidelines from the Infectious Disease Society of America



Clinical Infectious Diseases Advance Access published December 4, 2013

IDSA GUIDELINES

2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host

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An international panel of experts prepared an evidenced-based guideline for vaccination of immunocompromised adults and children. These guidelines are intended for use by primary care and subspecialty providers who care for immunocompromised patients. Evidence was often limited. Areas that warrant future investigation are highlighted.

- Areas not addressed by ACIP
- Some differences

Differences in IDSA / ACIP VACCINE –SPECIFIC Document

- IDSA: Recommendation for Gardasil (HPV) for Immunocompromise
- ACIP: No preference for Gardasil or Cervarix in immunocompromised females

- IDSA: Recommendation for Varicella vaccine for immunocompromised persons (within certain parameters)
- ACIP: Consideration for Varicella vaccine for immunocompromised persons (within certain parameters)

ACIP General Recs Altered Immunocompetence Draft

- Nothing in Draft violates an ACIP vaccine-specific document
- Any place where there is a deviation between IDSA and a vaccine-specific ACIP statement, it will have to be addressed
- This is the purview of the vaccine-specific ACIP WG, not General Recs
- Work ongoing to clarify these issues

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Altered Immunocompetence: Indications

- Primary source for changes: vaccine-specific ACIP statements
- NOT from IDSA document
- Vaccines included:
  - Pneumococcal Vaccines
  - Meningococcal Vaccines
  - Hib Vaccines

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Layout of Altered Immunocompetence

- **Vaccination with Inactivated Vaccines**

  Safety issues – inactivated vaccines safe with altered immunocompetence

  Efficacy issues – concerns with certain diseases

- **Vaccination with Live Attenuated Viral and Bacterial Vaccines**

Rubin, LG, Levin MJ, Ljungman P., et. Al. 2013 IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromised Host. Clin. Infect. Dis. 2014; 58: e-44-100.

Efficacy Issues: Inactivated Vaccines

- **Concerns with certain disease conditions:**
  - Page 4, Line 26
  - B-cell deficiency and receipt of immunoglobulin therapy
    - Withhold inactivated vaccines (and live vaccines)
  - Cancer therapy and receipt of anti-B cell therapy (e.g. rituximab)
    - Delay inactivated vaccines 6 months

Rubin, LG, Levin MJ, Ljungman P., et. Al. 2013 IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromised Host. Clin. Infect. Dis. 2014; 58: e-44-100.

Layout of Altered Immunocompetence

- **Vaccination with Live Attenuated Viral and Bacterial Vaccines**
  - Safety and Efficacy Concern

Vaccination with Live Viral and Bacterial Vaccines: Specific Conditions

- Page 5, Line 4
- Defects of Chronic Granulomatous Disease
  - Withhold live bacterial vaccine
- Other phagocyte deficiency diseases (leukocyte adhesion deficiency, Chediak-Higashi syndrome)
  - Withhold live bacterial and live viral vaccines
- Defects of interferon-gamma/interleukin-12 Axis)
  - Withhold live bacterial vaccines
- Defects of interferon-alpha or interferon-gamma
  - Withhold live bacterial and live viral vaccines

Rubin, LG, Levin MJ, Ljungman P., et. Al. 2013 IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromised Host. Clin. Infect. Dis. 2014; 58: e-44-100.

Table of Conditions: Page 11, Line 19

TABLE 13. Vaccination of persons with primary and secondary immunodeficiencies

Primary	Specific immunodeficiency	Contraindicated vaccines*	Risk-specific recommended vaccines*	Effectiveness and comments
B-lymphocyte (humoral)	Severe antibody deficiencies (e.g., X-linked agammaglobulinemia and common variable immunodeficiency)	OPV†Smallpox LAIV BCG Ty21a (live typhoid) Yellow fever	Consider varicella vaccination in isolated humoral immunodeficiency	The effectiveness of any vaccine is uncertain if it depends only on the humoral response (e.g., PPSV or MPSV4). IGIV interferes with the immune response to measles vaccine and possibly varicella vaccine.
	Less severe antibody deficiencies (e.g., selective IgA deficiency and IgG subclass deficiency	OPV† BCG Yellow fever Other live vaccines appear to be safe.	Pneumococcal Hib	All vaccines likely effective; immune response might be attenuated.
T-lymphocyte (cell-mediated and humoral)	Complete defects (e.g., severe combined immunodeficiency [SCID] disease, complete DiGeorge syndrome)	All live vaccines§,¶,**	Pneumococcal	Vaccines might be ineffective.
	Partial defects (e.g., most patients with DiGeorge syndrome, Wiskott-Aldrich syndrome, ataxia-telangiectasia)	All live vaccines§,¶,**	Pneumococcal Meningococcal Hib (if not administered in infancy)	Effectiveness of any vaccine depends on degree of immune suppression.
	Interferon-gamma/Interleukin 12 axis deficiencies	All live bacterial vaccines (All live vaccines contraindicated in Interferon-gamma or interferon-alpha deficiencies)		
Complement	Persistent complement, properdin, or factor B deficiency	None	Pneumococcal Meningococcal Hib	All routine vaccines likely effective.
Phagocytic function	Chronic granulomatous disease	Live bacterial vaccines§		
	Leukocyte adhesion defect, and myeloperoxidase deficiency.	Live viral and bacterial vaccines§¶	Pneumococcal	All inactivated vaccines safe and likely effective. Live viral vaccines likely safe and effective.
Secondary	HIV/AIDS	OPV† Smallpox	Pneumococcal Hib for persons younger than 19 years if they did not a dose after 14 months of age and	MMR, varicella, rotavirus, and all inactivated vaccines, including inactivated influenza, might be

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Hematopoietic Cell Transplant Patients

- Current ACIP recommendations refer to Tomblyn M, Chiller T, Eisele H, et. Al. *Biol Blood Marrow Transplant* 15:1143-1238;2009.

- ACIP recommended referencing this document for questions related to HCT (Feb. 25, 2009)

- IDSA now publishes recommendations for HCT in
  - Rubin, LG, Levin MJ, Ljungman P., et. Al. 2013 IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromised Host. Clin. Infect. Dis. 2014; 58: e-44-100.

HCT Patients – IDSA Document

- **Recommendations similar to Blood, Marrow Transplant 2009**
- **Recommendations identical for certain vaccines:**
  - PCV vaccines (3 doses 3 months post HCT – 4 week interval between doses, followed by PCV13 or PPSV23)
  - Zos, RV (not recommended post HCT)
- **Recommendations are Flexible**
  - Multiple options – use of pertussis containing vaccines
  - Alternatives allowed depending on whether patient received vaccine doses prior to HCT

HCT Patients (Adoption of ISDA Recommendations)

- Authors on IDSA document reflect collaboration with ACIP, ACIP Gen Rec WG, and authors on Blood, Marrow Transplant 2009.
- Important additions – recommend use of new vaccines which previously were optional or not recommended: HPV vaccine, Varicella vaccine (as long as immunocompetent, no Graft vs Host disease, and 24 months post HCT)

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Conditions or Drugs that Might Cause Immunodeficiency

- **New IDSA Classification of Degree of Immunodeficiency**
- **High-level:**
  - Cancer Chemotherapy
  - Two months after solid organ transplant rejection therapy is finished
  - Daily corticosteroid therapy with dose 20 mg or higher prednisone equivalent (or 2 mg/kg or greater) for 14 days or more
  - Receiving immune modulators such as TNF-alpha inhibitors or anti-B cell agents (rituximab)

Rubin, LG, Levin MJ, Ljungman P., et. Al. 2013 IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromist Hot. Clin. Infect. Dis. 2014; 58: e-44-100.

Conditions or Drugs that Might Cause Immunodeficiency

- New IDSA Classification of Degree of Immunodeficiency
- Low-level
  - Alternate dose corticosteroid therapy
  - Methotrexate, azathioprine or 6-mercaptopurine in doses as stated in ACIP Zoster Vaccine-specific statement

Rubin, LG, Levin MJ, Ljungman P., et. Al. 2013 IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromist Hot. Clin. Infect. Dis. 2014; 58: e-44-100.

Conditions or Drugs that Might Cause Immunodeficiency – INTERVAL FOLLOWING THERAPY

- **Low-dose – 1 month**
- **High-dose – 3 months unless otherwise stated**
  - Solid organ transplant anti-rejection – 2 months
  - Anti-B cell – 6 months

Rubin, LG, Levin MJ, Ljungman P., et. Al. 2013 IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromist Hot. Clin. Infect. Dis. 2014; 58: e-44-100.

Conditions or Drugs that Might Cause Immunodeficiency – INTERVAL FOLLOWING VACCINE

- **Live vaccines**
  - Consider withholding unless 4 weeks before beginning of therapy
  - Recommend withhold 2 weeks before beginning of therapy
- **Inactivated vaccines**
  - Recommend withhold 2 weeks before beginning of therapy

Rubin, LG, Levin MJ, Ljungman P., et. Al. 2013 IDSA Clinical Practice Guidelines for Vaccination of the Immunocompromist Hot. Clin. Infect. Dis. 2014; 58: e-44-100.

Vaccination Programs

Vaccination Programs (GR – 2011)

- Vaccination of Children and Adolescents
- Adult Vaccination
- Evidence-Based Interventions to Increase Vaccination Coverage
- Other General Programmatic Issues

Vaccination Programs – Changes by GRWG

- **Inclusion of Adult Vaccination Standards – discussed in the intro to the section**
- **Added a sentence to discuss Affordable Care Act**
  - "Effective for all health-plans drafted or updated after September 2010, the ACA requires plans to cover ACIP recommended vaccines without deductibles or copayments when delivered by an in-network provider."
- **Removal of cost-effectiveness information**
  - Document unbalanced – discussed only in the Adult section – historical reasons
  - Cost-effectiveness best discussed in Vaccine Specific Statements, not in General Recs

Vaccination Programs – Changes by GRWG

- Strategies Table
- Updated Based on Task Force for Community Preventive Services with current updates from The Community Guide.org/vaccine/index.html
- Remove the word "strongly" (now only states "Recommended")
- "Patient of family incentives or sanctions" previously was listed "insufficient evidence"
  - Patient or family incentives – recommended
  - Sanctions- not recommended

Strategies Table: Page 14, Line 1

TABLE 15. Recommendations regarding interventions to improve coverage of vaccines recommended for routine use among children, adolescents, and adults	
Intervention	**Recommendation**
Increase community demand for vaccination	
Client reminder or recall systems	Recommended
Requirements for entry to schools, child-care facilities, and colleges	Recommended
Community education alone	Insufficient evidence
Community-based interventions implemented in combination	Recommended
Clinic-based education	Insufficient evidence
Patient or family incentives	Recommended
Patient or family monetary sanctions	Insufficient evidence
Client-held medical records	Insufficient evidence
Enhance access to vaccination services	
Reducing out-of-pocket costs	Recommended
Enhancing access through the U.S. Department of Agriculture's Women, Infants, and Children program	Recommended
Home visits, outreach, and case management targeted to particularly hard to reach populations to increase vaccination rates	Recommended
Enhancing access at schools	Recommended
Expanding access in health care settings	Recommended as part of multicomponent interventions only
Enhancing access at organized child care centers	Recommended

Strategies Table: Page 14, Line 1

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Requirements for entry to schools, child-care facilities, and colleges	Recommended
Community education alone	Insufficient evidence

Next Steps

- DISCUSSION

- Document sent out for October 2014, with remainder of General Recommendations Document, for vote.

The General Recommendations Work Group

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