Biologics Safety Update: Vaccines, Shingles

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Vaccines

• Which vaccines are indicated
• Which vaccines are contraindicated
• Best time to administer
2011 EULAR vaccine recommendations

1. Assess vaccination status at initial work-up
2. Administer vaccines during stable disease
3. Avoid live attenuated vaccines
4. OK to vaccinate w/DMARDs, anti-TNFs; vaccinate before starting B-cell depletion
5. Flu vaccine (inactivated) should be strongly considered
6. Pneumovax should be strongly considered
7. Tetanus recommendation same as general population (RTX caveat)
8. HZ vaccine may be considered
9. HPV vaccine should be considered
10. Hyposplenism -> flu, pneumo, Hib, meningococcal C
11. HAV/HBV vaccine only if at risk
12. Travel recommendation same as general population (live attenuated caveat)
13. BCG not recommended

Flu Vaccine

• Every patient, every year
• Only contraindication is known allergy to vaccine component
• Live (nasal) vs inactivated (injection)
Tetanus/Diphtheria/Pertussis

• ACIP recommends all adults receive Td (tetanus booster) every 10 years.
• **ONE** Td booster should be replaced by Tdap
  – Adacel FDA approved ages 11-64
  – Boostrix FDA approved ages 10 and older
  – ACIP recommendations: use either one

Hepatitis A & B

• All patients should get a hepatitis remote at baseline
• Hepatitis A negative: vaccinate
  – Vaccine is inactivated; 2 injections 6 months apart
  – No contraindications except previous anaphylactic reaction to a vaccine
• Hepatitis B negative: vaccinate
  – Vaccine is inactivated; 3 injections (0, 1 month, 6 months)
  – No contraindications except previous anaphylactic reaction to a vaccine
Pneumovax

- PCV7, PCV13, PPSV23
  - PCV7 + 6 more serotypes = PCV 13
  - 12/13 PCV13 + 11 more serotypes = PPSV23
- ACIP PPSV23 recommendations: vaccination of adults at high risk aged 19–64 years at the time of diagnosis of the high-risk condition. A one-time revaccination dose of PPSV23 is recommended 5 years after the first dose for immunocompromised persons
- ACIP PCV13 recommendations: Adults with specified immunocompromising conditions who are eligible for pneumococcal vaccine should be vaccinated with PCV13 during their next pneumococcal vaccination opportunity.

If never vaccinated, easy:
- PCV13 ASAP
- PPSV23 #1 at least 8 weeks after PCV13
- PPSV23 #2 5 years after PPSV23 #1

Two previous doses of PPSV23:
- PCV13 at least one year after last PPSV23

One previous dose of PPSV23:
- PCV13 at least one year after last PPSV23
- 2nd PPSV23 at least 8 weeks after PCV13 and at least 5 years after 1st PPSV23
VZV (Shingles) Incidence

- 1 million in US yearly
- 1-4/1000
  - 10/1000 >60
  - 15-91/1000 SLE
  - 10-15/1000 RA
  - 45/1000 GPA(WG)

- Incidence is increased with dialysis, glucocorticoid treatment and immunosuppressives
- Treatments for shingles do not prevent many important complications

Complications of Herpes Zoster

- Herpes Zoster Ophthalmicus
  - ~15% of HZ cases
  - Can occur when ophthalmic division of trigeminal nerve is involved
  - Untreated, 50-70% develop acute ocular complications
  - Can lead to chronic ocular complications, reduced vision, even blindness
- Neurologic complications
  - Myelitis, encephalitis, ventriculitis, meningoencephalitis, cranial nerve palsies, ischemic stroke syndrome
- VZV viremia
- Cutaneous dissemination, pneumonia, hepatitis, disseminated intravascular coagulation
- Dermatologic complications
- Secondary infections of rash
- Permanent scarring and changes in pigmentation
Complications of Herpes Zoster: Postherpetic Neuralgia (PHN)

- Pain ≥ 30 days occurs in 18-30% of zoster cases
- Mild to excruciating pain after resolution of rash
- Constant, intermittent, or triggered by trivial stimuli
- May persist weeks, months or occasionally years
- Can disrupt sleep, mood, work, and activities of daily living and lead to social withdrawal and depression
- Risk factors for PHN include age ≥ 50, severe pain before or after onset of rash, extensive rash, and trigeminal or ophthalmic distribution of rash

Herpes Zoster Vaccine

- Licensed in 1996
- Live, attenuated VZV
- Same strain used in the varicella vaccine, but 14x more potent
- Administered subcutaneously in deltoid region
Efficacy of Herpes Zoster Vaccine

- Decreased zoster incidence by 51%
- Decreased risk of post-herpetic neuralgia in all participants by 67%
- Decreased burden of illness (severity x duration) in all participants by 61%

ACIP Recommendations for Zoster Vaccine

- In October 2008, the Advisory Committee on Immunization Practices (ACIP) recommended a dose of the herpes zoster vaccine (HZV) for all adults ≥60 years of age unless they have contraindications.
  - Note: In March 2011 the FDA approved Zostavax for persons age 50-59.
- HZV should be offered at the patient’s first available clinical encounter

ACIP Recommendations for Zoster Vaccine

• HZV can be administered simultaneously with influenza and pneumococcal vaccines
• HZV is recommended whether or not the patient reports a prior episode of zoster
• It is not necessary to check varicella history or titers before administering HZV
• HZV should be offered to eligible persons including those >80 y.o., frail, or with chronic illnesses

Contraindications for Zoster Vaccine

• Immunosuppression (high-dose steroids, biological response modifiers, chemotherapy, AIDS) is a contraindication for HZV
  – Rheum-specific guidelines per ACR Hotlines
• HIV-positive status alone is not an contraindication
• Persons ≥60 y.o. anticipating immunodeficiency due to initiation of treatments or progression of illness should be offered HZV
**Update on Herpes Zoster (Shingles) Vaccine for Autoimmune Disease Patients**

- RA pts have a 1.5 to 2 fold increased risk for shingles.
- ACR recommends the vaccine for older RA patients receiving non-biologic DMARD therapies, or before DMARD or biologic treatments are started.
- CDC has recommended that pts receiving lower dose prednisone (< 20 mg/day) or MTX / AZA at doses used for rheumatic diseases may safely receive the vaccine.
- The vaccine is currently considered inadvisable for patients treated with biologic therapies. May be reasonable to hold the biologic for a period of time, vaccinate, and resume the biologic approximately 30 days later.
- Observational data suggests that the effectiveness of the vaccine in patients with autoimmune diseases is comparable to that in healthy, older patients. The vaccine was not associated with short term risks for zoster or varicella, even in pts exposed to biologics around the time they were vaccinated. However, in the absence of a prospective trial, this evidence should not be presumed to supersede the cautions regarding live virus vaccines in biologic users.
- The duration of long-term immunity conferred by an episode of shingles or the zoster vaccine is not clear, so it may be reasonable to vaccinate even people who have had shingles in the past (e.g. >= 5 years ago).

**CDC**

- If patients already on immunosuppression:
  - Defer zoster vaccine at least 1 month after discontinuation of high-dose prednisone (>20 mg per day)
  - Defer zoster vaccine at least 1 month after discontinuation of anti-TNF
Herpes Zoster Vaccination Coverage:
U.S., Age 60 or Older, 2007-2009

![Graph showing Herpes Zoster Vaccination Coverage]

5 Lindley M, Harpaz R, Bialek S. Awareness and Uptake of Zoster Vaccine among U.S. Adults ≥60 Years. Presented at National Immunization Conference; 2010 April 19–22; Atlanta, GA. Available at: http://cdc.confex.com/cdc/nic2010/recordingredirect.cgi/id/6765

Bottom Line: Vaccines and Rheumatology

- Patients often come into the rheumatology setting as candidates for vaccinations.
- We are very good at putting them at risk for more frequent and more severe cases of vaccine-preventable illnesses due to immunosuppression.
- We are not so good at protecting them before immunosuppression.
- There is room for improvement – assess vaccine status at first encounter and vaccinate as soon as safely possible.
Case Study: Vaccines

• 55 year old male
• CCP+ erosive RA recently diagnosed
• On 20 mg prednisone per day x6 weeks
• Started MTX 2 weeks ago. Dose now is 12.5 mg per week.

Case Study: Vaccines

• Immunization History
  – Had his flu shot this year
  – Thinks he had one dose of a pneumonia vaccine
  – Last tetanus booster was at an Urgent Care 4 years ago when he cut himself in his garage workshop
Case Study: Vaccines

• Relevant Labs:
  – Hep A surface Ab negative
  – Hep B core and surface antibody negative
  – IGRA negative

Question 1

• Does the patient need further pneumococcal vaccination at this time?
  – A. Yes, he needs PPSV 23 now
  – B. Yes, he needs PPV 13 now
  – C. No, he needs to wait until he’s 60
  – D. No, he cannot get any pneumovax until his prednisone dose is lower
Question 2

• Does he need a tetanus shot?
  – A. Yes, he needs Tdap
  – B. Yes, he needs Td
  – C. No, he just got one 4 years ago
  – D. Maybe

Question 3

• What hepatitis vaccines is he eligible for?
  – A. Hepatitis A
  – B. Hepatitis B
  – C. Hepatitis C
  – D. A & B
  – E. A & B & C
Question 4

- What, if anything, should be done about a shingles vaccine?
  - A. Nothing now due to prednisone
  - B. Vaccinate today
  - C. Check varicella titers and if low, prepare to vaccinate as soon as possible
  - D. Nothing now due to the fact that no biologic is planned