Before It’s Too Late... Post Exposure Prophylaxis

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Objectives

• Differentiate events and exposures that require post exposure prophylaxis from those that do not
• Outline the use of vaccines in adults to eradicate certain diseases
• Evaluate the need for the administration of newer vaccines
• Given a patient case, determine appropriate vaccine and/or hyperimmune therapy

Disclosure Statement

Name of Presenter:
John Marshall, PharmD, BCPS
Speaker has no actual or potential conflict of interest in relation to this program.
Speaker does not plan on discussing unlabeled/investigational uses of a commercial product and will disclose this to the audience.
Topics

• Review of immunization modalities (vaccines, immune globulins, toxoids)
• Review of active and passive immunization
• Focus on common exposures:
  – Rabies
  – Tetanus/Tdap
  – Hepatitis A/B

Immunization Modalities

• Vaccines: derived from the infecting organism
  – Viral:
    • Live attenuated
    • Killed (fragments/particles) - may require booster doses
  – Bacterial
    • Killed whole bacteria
    • Bacterial wall antigens
• Toxoids: inactivated bacterial toxins that stimulate the formation of antitoxin

Immunization Modalities

• Immune Sera: Antibody derived from human sources
  – Non-specific (IVIG)
  – Disease-specific (rabies, tetanus, hepatitis B)
• BOTH vaccines and toxoids produce active immunity, while immune sera produce passive immunity
### Active and Passive Immunity

<table>
<thead>
<tr>
<th>Active Immunity</th>
<th>Passive Immunity</th>
</tr>
</thead>
<tbody>
<tr>
<td>• May take 7-10 days to detect antibodies</td>
<td>• Acts immediately</td>
</tr>
<tr>
<td>• Most often permanent</td>
<td>• Temporary (days-weeks)</td>
</tr>
<tr>
<td>• May be inhibited by passive immunization (e.g. MMR with IVIG or maternal antibodies)</td>
<td>• Human immune serum globulin (IVIG, IMIG)</td>
</tr>
<tr>
<td>• Caution administration in immunocompromised</td>
<td>• Specific immune globulins targeted at a specific agent</td>
</tr>
<tr>
<td></td>
<td>• Animal sera/antitoxins</td>
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</tbody>
</table>

### Rabies

- Rabies is an acute progressive (and fatal) encephalomylitis caused by the RNA viruses in the family Rhabdoviridae
- Around 50,000 people die yearly of rabies worldwide
  - Whereas in the U.S., there are on average two cases of human rabies per year
  - 61 cases diagnosed from 1980-2006
  - Since 2000, 24 reported human cases
    - Of which, 23 died subsequent to infection
    - Rabies is found throughout the U.S. except Hawaii

Blanton JD, Horne CA, Rupprecht CE. JAVMA 2007; 231: 540-556

### Rabies

- A recent study has demonstrated that inappropriate prophylaxis was given in 40% of cases
  - Inappropriate in 40% of patients to whom it was given
    - Most common mistake was that the animal was available for testing
  - Inappropriately withheld in 6.3% of patients
    - Most common mistake was exposure in high endemic areas from an animal unavailable for testing

Assessment of Risk

- Type of Exposure
  - Bite - Majority of exposures. Risk increases with the number of bites and bites closer to the CNS
  - Non-bite exposure (Two conditions must be met)
    1. Exposure must be to the mucous membranes or open wounds
    2. Animal tissues making contact must be potentially infectious (i.e., saliva, neural tissue); blood/feces don’t count
  - Provoked vs. Unprovoked
  - Type of animal

Rabies... Who are the Suspects?

- Bats
- Carnivore or larger animal (raccoon, fox, skunk, coyote, beaver, woodchuck)
- Domestic animals (dog, cat, ferret, livestock)
- Small animal/rodent (squirrel, rat, mouse, rabbit) -- almost never

Wildlife Carriers

Acute Treatment/Post Exposure Prophylaxis

- A medical URGENCY not EMERGENCY
- Wound care: Thorough washing with a virucidal agent (povidone iodine)
- Isolation of the animal
- Timing: As soon as possible, but latency periods of 1-7 years have been reported
- Patients with previous rabies vaccination
  - 2 doses of vaccine day 0 and 3
  - Rabies immune globulin should not be administered
Post Exposure Prophylaxis

- Not previously vaccinated:
  - 4 doses of rabies vaccine: days (0,3,7,14) (previously 5 doses)
  - Give in deltoid in adults, anterolateral thigh in children
  - 5 Doses should be given to immunosuppressed patients
- Rabies Immune Globulin
  - 20 IU/kg single dose
  - Infiltrate in and around the wound as much as possible, then administer the remainder IM at a site distant from vaccine administration.
  - Do not give if exposure >7 days prior
  - Do not give other live vaccines within 3 months (MMR)

Vaccine ADR

- Most common:
  - Injection site pain, redness, swelling
- Mild systemic reactions – fever, headache, dizziness
- Systemic hypersensitivity reactions following booster – 6%

Case 1:

JV is a 28 year old female who presents to the emergency department after being scratched by a squirrel. She states that the incident occurred while she was walking her dog in the park. She describes that the dog lunged into a bush, causing the squirrel to jump at which point it collided with her causing a small, superficial abrasion on her cheek. She has no history of rabies vaccination.

Assess the need (and agents if necessary) for post exposure prophylaxis in this patient.
Case 2:
JM is a 36 year old white male who presents to the emergency department after being chased by a fox in his front yard 2 hours ago. He states that the fox came from across the street and was nipping at his feet. He was able to scare the fox away with a stick, but not before the fox nipped his shin through his pants, causing a small, superficial abrasion. He has no previous history of rabies vaccination.

Assess the need (and agents if necessary) for post exposure prophylaxis in this patient.

Tetanus
- Neurologic disorder characterized by increased muscle tone.
- Caused by a protein (tetanospasmin) elaborated by Clostridium tetani
- Usually acquired through puncture wounds, lacerations, or abrasions
- Vaccination is through the administration of a toxoid (inactivated biological toxin)

Tetanus
- Primary vaccination series (adults):
  - 3 doses: First and second dose separated by 1 month, 3rd dose 12 months later
  - Booster doses are given every 10 years
High-risk populations

• Elderly patients:
  – Age related decline in protection against tetanus (<30% in adults older than 70 yrs)
  – Patients older than 60 account for 60% of all cases of tetanus

• Those born outside of the United States:
  • Mexican Americans: <60% immunity rate
  • Korean Americans: <20% immunity rate

• Patients with diabetes
  – Account for approx. 13% of all cases and 29% of all deaths

Tetanus

• Post exposure prophylaxis therapy is dependant on the vaccination status of the patient
  – Primary series
  – Uncertain or incomplete primary series

• Puncture wounds are highest risk, followed by deep lacerations

Tetanus Immune Globulin

• Given to patients with questionable immunization history with high risk wounds

• Dose:
  – 250 Units IM x 1 (prophylaxis)
  – 3000-6000 Units (treatment)

• Must give in a different syringe at a different site from Td or DT
### Prophylaxis

<table>
<thead>
<tr>
<th>History of previous tetanus immunization</th>
<th>Clean, minor wounds</th>
<th>All other wounds (wounds contaminated with dirt, feces, soil and saliva, puncture, crushing, burns and frostbite wounds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncertain or fewer than 3 doses</td>
<td>Give vaccine only</td>
<td>Give vaccine and tetanus immune globulin</td>
</tr>
<tr>
<td>3 or more previous doses</td>
<td>No need to vaccinate, unless ≥10 years since last dose</td>
<td>Give vaccine if ≥5 years since last dose</td>
</tr>
</tbody>
</table>

American College of Physicians Task Force on Adult Immunization and IDSA. Guide for Adult Immunization. 1994

### Pertussis (Whooping Cough)

- Characterized an acute, infectious cough due to a gram negative organism (*B. pertussis*)
- Immunity wanes 5-10 years post vaccination
- 2005 – A product was licensed in US to prevent pertussis in adults (Tdap)

### Pertussis—United States, 1980-2002

- Graph showing cases of pertussis from 1980 to 2002, with a significant increase in the mid-1990s.
DTaP vs Tdap – BE CAREFUL!

- DTaP
  - For children 6wks-6yr
  - Has higher antigen concentration of Diptheria and Pertussis
  - Meant for active immunization
  - Daptacil, Tripedia, Infanrix

- Tdap
  - Older children, adolescents, adults
  - Lower concentrations of diptheria and pertussis
  - Meant as a booster
  - Boostrix, Adacel

What may happen if an adult were to get DTaP?
What may happen if a child were to get Tdap?

Tdap

- Who should be receiving Tdap:
  - Adults 19-64 for their next tetanus booster
  - Adults with close infant (<12mo) contact.
    - An interval of 2 years is recommended
  - Postpartum women who have not received Tdap
  - Healthcare workers with patient contact
    - 2 year interval

Case 1.1:
JV is a 28 year old female who presents to the emergency department after being scratched by a squirrel. She states that the incident occurred while she was walking her dog in the park. She describes that the dog lunged into a bush, causing the squirrel to jump at which point it collided with her causing a small, superficial abrasion on her cheek. She has no history of rabies vaccination, and her last tetanus immunization was 4 years prior.

Assess the need (and agents if necessary) for post exposure prophylaxis in this patient.
Case 2.1:
JM is a 36 year old white male who presents to the emergency department after being chased by a fox in his front yard 2 hours ago. He states that the fox came from across the street and was nipping at his feet. He was able to scare the fox away with a stick, but not before the fox nipped his shin through his pants, causing a small, superficial abrasion. He has no previous history of rabies vaccination, and his last dose of tetanus toxoid was 14 years prior.

Assess the need (and agents if necessary) for post exposure prophylaxis in this patient.

Hepatitis A
- RNA virus that can produce asymptomatic or symptomatic infection in humans
  - Jaundice, fatigue, nausea, diarrhea, fever
- No chronic (long term) infection
- Spread through fecal-oral route
- Found in the stool of persons with hepatitis A

Hepatitis A
- Persons at Risk:
  - Household contacts of infected persons
  - Sexual contacts of infected persons
  - People (esp children) living in areas with increased rates of hepatitis A
  - Persons traveling to countries where hepatitis A is common
  - Men who have sex with men
  - Injecting and non-injecting drug users
Hepatitis A

• Vaccine – Not for post-exposure
  – Two formulations VAQTA, HAVIRX
    • Both are inactivated viral vaccines
    • May be interchanged if necessary
  – Given as two doses at 0 and 6-12 months
    • Children 2-18 get ½ of the adult dose
  – Protection is achieved approximately 4 weeks after first dose (94-100% will have protective antibody titers)
    • 2nd dose given to ensure long-term immunity

Hepatitis A

• Immune Globulin (IGIM)
• Given to patients exposed to a documented source of Hepatitis A (eg food worker)
  – 0.02ml/kg will provide protection in up to 85% of patients
    • The earlier the administration, the better
    • No use if exposure >2 weeks prior
  – Caution co-administration with other live vaccines (MMR, Varicella)
Hepatitis B

- Double stranded DNA virus
- Replicates in the liver, may cause acute and chronic hepatitis
  - Highest concentration in the blood, but also in serum derived body fluids
  - Incubation period: 45-160 days
- 300 million HBV carriers in the world

Risk Factors for HBV infection

- Household contact of hepatitis B patient: 2%
- Medical employee: 1%
- Sexual contact with hepatitis B patient: 13%
- Men who have sex with men: 6%
- Injection drug use: 14%
- Multiple sex partners: 17%
- Hemodialysis: 0%
- Unknown: 32%
- Other: Surgery, dental surgery, acupuncture, tattoo, other percutaneous injury

http://www.cdc.gov/ncidod/diseases/hepatitis/index.htm
Hollinger, FB Gut 1966; 38:24S
Gerberding JL NEJM 1996; 334:594
Hepatitis B

• Modes of Transmission:
  – Perinatal
  – Horizontal (most likely in children) via minor breaks in the skin or mucus membranes
    • Toothbrushes
    • Toys
  – Unprotected sexual intercourse (50% of transmission in US)
  – Nosocomial: Most commonly transmitted blood borne virus in the healthcare setting
    • Accidental needlestick
    • Contaminated instruments

Risk of Infection

• Adults with normal immune status:
  – 94-98% will recover completely from newly acquired Hepatitis B infections, eliminating virus from blood and producing antibodies

Infants
Young Children
Immunosuppressed patients

Newly acquired Hep B virus more likely to result in chronic infection

Hepatitis B – New Approaches

• Immigrants to US have a higher prevalence, and thus need special consideration
  – Preventing perinatal transmission
  – Vaccinating children in high risk groups
  – Routine vaccination of all children born
  – Vaccinating adults in high risk groups (IVDA etc)
Hepatitis B Vaccine

- 1 ml IM (deltoid) at 0, 1, and 6 months (adults)
- Check Antibody titer 1-6 months after series
  - Responder: >10mIU/ml anti-HepB surface antigen (anti-HBs)
  - Non-Responder: <10mIU/ml anti-HBs
- Risk factors for failure to respond:
  - Obesity
  - Smoking
  - Age>50
  - Immunosuppressed
- First dose of vaccine should be administered within 12 hours of exposure

Hepatitis B Immune Globulin (HBIG)

- Prepared from human plasma
- Dose: 0.06 ml/kg IM
- Indication for use dependant on prior history of immunization and documented response of exposed person
- Given in perinatal setting to prevent maternal transmission to infant
- Effectiveness when given more than 7 days post exposure is lacking

Hep B Prophylaxis

<table>
<thead>
<tr>
<th>Vaccination history and antibody response of exposed</th>
<th>Source is HBsAg+ (indicates active hep B)</th>
<th>Source is HBsAg-</th>
<th>Source not tested or unknown status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown vaccination</td>
<td>HBIG + vaccine series</td>
<td>Vaccine series</td>
<td>Vaccine series</td>
</tr>
<tr>
<td>Previously vaccinated</td>
<td>No treatment necessary</td>
<td>No treatment</td>
<td>No treatment necessary</td>
</tr>
<tr>
<td>Known responder</td>
<td>No treatment necessary</td>
<td>No treatment</td>
<td>No treatment necessary</td>
</tr>
<tr>
<td>Known non-responder</td>
<td>HBIG + vaccine series</td>
<td>No treatment</td>
<td>If high risk source, treat like HBsAg+</td>
</tr>
<tr>
<td>Unknown antibody response</td>
<td>Test exposed person and follow above</td>
<td>No treatment</td>
<td>Test exposed person and follow above</td>
</tr>
</tbody>
</table>

American College of Physicians Task Force on Adult Immunization and IDSA. Guide for Adult Immunization. 1994
Case 3

FP is a 38 year old woman who presents to the emergency department after reading that a sandwich shop she frequents has reported a worker testing positive with “some sort of hepatitis.” Her last visit to the shop was 2 days prior, and she currently complains of fatigue and jaundice.

Assess the need (and agents if necessary) for post exposure prophylaxis in this patient.

Case 4:

VA is a 56 year old ICU nurse who presents to the employee health department of the hospital after an accidental needle stick from a patient she was caring for in the ICU. She states that the needlestick occurred after she was drawing blood cultures and the patient suddenly jerked, causing the needle to stick in her right index finger. The patient is a known hepatitis B carrier (HBsAg positive). The nurse has received the primary hepatitis B vaccination series, and a titer performed 5 months after her series was found to be 5 mIU/ml anti HBs. VA had a tetanus booster 6 years prior.

Assess the need (and agents if necessary) for post exposure prophylaxis in this patient.

Points to Remember

- Many times post exposure prophylaxis does not require the administration of passive immunity
- Certain patient populations (elderly, children, immunosuppressed, immigrant) are at greater risk and should be given special consideration
- When administering passive and active immunity, give injections at different sites
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