Hot Topics in Infectious Diseases

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Disclosure Information

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• I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.

• I acknowledge that today’s activity is certified for CME credit and thus cannot be promotional. I will give a balanced presentation using the best available evidence to support my conclusions and recommendations.
Objectives

• To learn through a series of cases of children presenting with infectious diseases new or emerging pathogens and/or new methods to diagnose and manage infectious diseases in children
Red Hot Topics
Influenza Vaccine Recommendations for 2018-2019
Case 1

A previously healthy 10 year old girl presents to your office for her routine health maintenance visit in September 2018.

What influenza vaccine should she be given?

A. Trivalent IIV  
B. Quadrivalent IIV  
C. Quadrivalent LAIV  
D. Either A or B  
E. Either A, B or C
Influenza Vaccines for the 2018-2019 Season

• 2018–19 trivalent vaccines contain:
  – an A/Michigan/45/2015 (H1N1) pdm09-like virus
  – an A/Singapore/INFIMH-16-0019/2016 (H3N2)-like virus
  – a B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage)

• 2018-2019 quadrivalent vaccines have two influenza B viruses and contain:
  – the viruses recommended for the trivalent vaccines
  – a B/Phuket/3073/2013-like virus (B/Yamagata lineage)
ACIP Recommendations

• Recommends that all patients ages 6 months and older without contraindications should receive influenza vaccine during the 2018-19 influenza season

• Clinicians may administer any licensed, age-appropriate influenza vaccine, including LAIV (for patients ages 2-49 without contraindications), inactivated influenza vaccine and recombinant influenza vaccine
AAP Recommendations

- Recommends IIV for children in the 2018-2019 season as it has been more consistently effective against most strains of flu in recent seasons
- LAIV may be an option for children who otherwise will not be vaccinated
Why should we vaccinate?

- 174 pediatric deaths from influenza were reported this past season
  - about 80% of the children who died were not vaccinated
Prepare for the Upcoming Flu Season

- Initiate team meetings on the following topics:
  - Discuss what worked or didn't work in the office this past season
  - Determine what improvements might be made to increase influenza immunization rates
  - Develop or update written infection control measures or office protocols for minimizing transmission of influenza and other infectious diseases
  - Plan and schedule staff training on standard precautions, infection control, seasonal and pandemic influenza, and the importance of immunization
Suggested Reading

• Centers for Disease Control and Prevention. Vaccine effectiveness - How well does the flu vaccine work?

• CDC’s seasonal influenza web page for health professionals, www.cdc.gov/flu/professionals/index.htm
Management of Skin and Soft Tissue Infections
SSTI Case 1

• A 3-year-old boy developed a lesion that looked like spider bite on his legs. His parents and siblings had similar lesions.

• What would be the most appropriate initial management?
  A. Clindamycin
  B. I&D
  C. I&D plus TMP-SMX
  D. TMP-SMX
  E. Warm Soaks
IDSA Clinical Care Guidelines for Treatment of MRSA

- Consensus guidelines from a panel of experts
- Published in 2011
- Reviewed all available evidence on treatment of MRSA infections in adults and children

For a cutaneous abscess, I&D is the primary treatment

For simple abscesses or boils, I&D alone is likely to be adequate

Additional data are needed to further define the role of antibiotics, if any, in this setting
Do Antibiotics Facilitate More Rapid Resolution than I&D Alone in the Management of Small Skin Abscesses?

- Limited data on the role of antimicrobials in the treatment of skin abscesses undergoing I&D
- Study to answer this question published in 2017
- Daum and colleagues looked at short-term outcomes in patients who have a small skin abscess
  - Participants with a skin abscess 5 cm or smaller in diameter were enrolled
  - After abscess I&D, participants randomly assigned to receive clindamycin, TMP-SMX, or placebo for 10 days
  - The primary outcome was clinical cure 7 to 10 days after the end of treatment

Do Antibiotics Facilitate More Rapid Resolution than I&D Alone in the Management of Small Skin Abscesses?

• Results
  – Enrolled 786 participants
    • 64% adults and 36% children
  – *S. aureus* isolated from 67% of participants
    • MRSA in 49%
  – Cure rates
    • Clindamycin group (83.1%)
    • TMP-SMX group (81.7%)
    • Placebo group (68.9%)
  – Beneficial effect was restricted to those with *S. aureus*

Do Antibiotics Facilitate More Rapid Resolution than I&D Alone in the Management of Small Skin Abscesses?

• Conclusions
  • As compared with I&D alone, clindamycin or TMP-SMX in conjunction with I&D improves short-term outcomes in patients who have a simple abscess
  • This benefit must be weighed against the known side-effects of these antibiotics

SSTI Case 1 Revisit

- A 3-year-old boy developed a lesion that looked like spider bite on his legs. His parents and siblings had similar lesions.

- What would be the most appropriate initial management?
  A. Clindamycin
  B. I&D
  C. I&D plus TMP-SMX
  D. TMP-SMX
  E. Warm Soaks
SSTI Case 2

- A 6-year-old girl presents to the ED with right arm redness and swelling of two days duration
- On exam she is afebrile and has an area of erythema, swelling and tenderness over her right elbow
What would you start?

A. Cephalexin
B. Cephalexin plus TMP-SMX
C. Clindamycin
D. TMP-SMX
IDSA Clinical Care Guidelines for Outpatients with Nonpurulent Cellulitis

• No purulent drainage or exudate and no associated abscess

• Empiric therapy for GABHS is recommended

• Empiric coverage for CA-MRSA
  – Recommended if no response to β-lactam therapy
  – Consider if systemic toxicity

• Five to 10 days of therapy is recommended
• If coverage for both GABHS and CA-MRSA is desired, options include the following:
  – clindamycin alone (MRSA, MSSA and GABHS may be resistant)
  – a tetracycline or TMP-SMX in combination with a β-lactam
  – linezolid alone
Although prescribing antimicrobials with activity against MRSA may be reasonable in some cases of skin and soft tissue infection, it is likely that the pendulum has swung too far in the direction of covering empirically for MRSA “just in case.”
Is Cephalexin Plus TMP-SMX Needed for Clinical Cure of Nonpurulent Cellulitis without Abscess?

- Study to answer this question published in 2017
- The investigators randomly assigned 500 patients with cellulitis who presented to 5 EDs to receive a 7-day course of
  - cephalexin and TMP-SMX or
  - cephalexin and placebo
- All patients underwent ultrasound to exclude abscess at study entry

Is Cephalexin Plus TMP-SMX Needed for Clinical Cure of Nonpurulent Cellulitis without Abscess?

• Results
  – No significant difference in the clinical cure rate at 14 to 21 days
    • cephalexin plus TMP-SMX group 83.5%
    • cephalexin plus placebo group 85.5%
  – No difference in need for additional antibiotics or surgical drainage
  – No patients developed an invasive infection
• Patients in both groups who experienced treatment failure
  – more than half developed clinical evidence of abscess, for which the primary therapy is drainage
• The results of this study indicate that
  – most patients presenting with nonpurulent cellulitis without abscess can be safely treated without the addition of antibiotics directed against MRSA

A 6-year-old girl presents to the ED with right arm redness and swelling of two days duration.

On exam she is afebrile and has an area of erythema, swelling and tenderness over her right elbow.
What would you start?

A. Cephalexin
B. Cephalexin plus TMP-SMX
C. Clindamycin
D. TMP-SMX
IDSA Clinical Care Guidelines for Outpatients with Purulent Cellulitis

- Cellulitis associated with purulent drainage or exudate in the absence of a drainable abscess
- Culture exudate
- Empiric therapy
  - Cover for CA-MRSA pending culture results
  - GABHS coverage not needed
- Five to 10 days of therapy is recommended
  - Individualize based on the patient’s clinical response
Microbiology of Purulent Cellulitis

- MRSA 59%
- MSSA 17%
- B-hemolytic strep 3%
- non-B hemolytic strep 4%
- other 8%
- unknown 9%

Moran NEJM 2006; 355: 666-74
• Oral antibiotic options include the following:
  – Clindamycin
  – TMP-SMX
  – A tetracycline (doxycycline or minocycline)
  – Linezolid


Management of Needle Stick Injuries
Needle Stick Injury Case

• A 5 year old male is brought to your office by his mother. While playing at a public beach he picked up a discarded 1 mL syringe with an attached 27 gauge needle and punctured the skin on his hand. His mother is very upset and is afraid her son will catch AIDS.

• What is the risk of transmission of a blood-borne virus by this needlestick?

• How should you manage this patient?
Needlestick Injuries are Increasing Due to the Opioid Epidemic

Heroin crisis rains needles on streets, beaches - The Providence Journal, 2017-07-18

By Michael Casey
The Associated Press

LOWELL, Mass. — They hide in weeds along hiking trails and in playground grass. They wash into rivers and float downstream to land on beaches. They pepper baseball dugouts, sidewalks and streets. Syringes left by drug users amid the heroin crisis are turning up everywhere.

In Portland, Maine, officials have collected more than 700 needles so far this year, putting them on track to handily exceed the nearly 900 gathered in all of 2016. In March alone, San Francisco collected more than 13,000 syringes, compared with only about 2,000 the same month in 2016.

People, often children, risk getting stuck by discarded needles, raising the prospect they could contract blood-borne diseases such as hepatitis or HIV or be exposed to remnants of heroin or other drugs.

It’s unclear whether anyone has gotten sick, but the reports of children finding the needles can be sickening in their own right. One 6-year-old girl in California mistook a discarded syringe for a thermometer and put it in her mouth; she was unharmed.

“I just want more awareness that this is happening,” said Nancy Holmes, whose 11-year-old daughter stepped on a needle in Santa Cruz, California, while swimming. “You would hear stories about finding needles at the beach or being poked at the beach. But you think that it wouldn’t happen to you. Sure enough.”

They are a growing problem in New Hampshire and Massachusetts, two states that have seen many overdose deaths in recent years.

“We would certainly characterize this as a health hazard,” said Tim Sweeney, health director in Manchester, New Hampshire’s largest city, which collected 570 needles in 2016, the first year it began tracking the problem. It has found 247 needles so far this year.

Needles turn up in places like parks, baseball diamonds, trails and beaches — isolated spots where drug users can gather and attract little attention, and often the same spots used by the public for recreation. The needles are toxic to both children and pets.

“Someone or something must be manipulating or disposing of them improperly,” said an official.

One child was poked by a needle left on the grounds of a Utah elementary school. Another youngster stepped on one while playing on a beach in New Hampshire.

Even if adults or children don’t get sick, they must endure an unsettling battery of tests to make sure they didn’t catch anything. The girl who put a syringe in her mouth was tested and had to be tested for hepatitis B and C, her mother said.

Some community advocates are trying to sweep up the pollution.

Rocky Morrison, a spokesman for the Merrimack River, which winds through the old milling city of Lowell, and has recovered hundreds of needles in abandoned homeless camps that dot the banks, as well as in piles of debris that collect in floating booms he recently started setting.

He has collected a collection of several hundred needles in a fishbowl, a prop he uses to illustrate that the problem is real and that towns must do more to combat it.

“We started seeing it last year here and there. But now, it’s just raining needles everywhere we go,” said Morrison, a 49-year-old construction worker. “The stuff comes from somewhere. If we can work together to stop it at the source, I am all for it.”

Among the oldest tracking programs is in Santa Cruz, California, where the community group Take Back Santa Cruz has reported finding more than 14,500 needles in the county over the past 4 1/2 years. It says it has gotten reports of 12 people getting stuck, half of them children.

“It’s becoming pretty commonplace to find them. We call it a rite of passage for a child to find their first needle,” said Gabrielle Korte, a member of the group’s needle team.

Along the Merrimack, nearly three dozen riverfront towns are debating how to stem the flow of needles. Two regional planning commissions are drafting a request for proposals for a cleanup plan. They hope to have it ready by the end of July.

“We are all trying to get a grip on the problem,” said Fuvrehill Mayor James Fiorini. “The stuff comes from somewhere. If we can work together to stop it at the source, I am all for it.”
Management of Case

• Clean wound thoroughly with soap and water as soon as possible
  – no evidence for use of antiseptics or bleach
• Assess the extent of the wound
• Determine the child’s immunization status for tetanus and HBV
• Tetanus vaccine, with or without tetanus immune globulin, should be given if indicated.
Management of Case

• Document the circumstances of the injury
  – the date and time of injury
  – where the needle was found
  – circumstances of the injury
  – type of needle
  – whether there was a syringe attached
  – whether visible blood was present in or on the needle or syringe
  – whether the injury caused bleeding
  – whether the previous user of the needle is known
Assess Type of Exposure to Quantify Risk

- The type of needle
  - hollow bore vs. solid bore
  - small gauge (diabetic) vs. larger gauge (drug injection)
- The severity of the needle stick
  - superficial vs. deep
- The presence of visible blood on the needle and on the skin
- Volume of blood transferred
Management of Case

• If the user of the needle is known
  – Make attempt to assess for risk factors for blood-borne viruses and, if possible, test for these viruses
  – Pending results, proceed as for an unknown source
Case

- From information provided percutaneous exposure occurred to a needle perhaps used to inject recreational drugs
- HIV seroconversion after a needle stick is uncommon - precise seroconversion risk for this child cannot be accurately stated
- More likely to acquire hepatitis B or C
Risk of HIV from Needlestick Exposure in the Hospital Setting

<table>
<thead>
<tr>
<th>Exposure type</th>
<th>Rate for HIV acquisition per 10,000 exposures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral</td>
<td></td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>9,250</td>
</tr>
<tr>
<td>Needle sharing during injection drug use</td>
<td>63</td>
</tr>
<tr>
<td>Percutaneous (needlestick)</td>
<td>23</td>
</tr>
</tbody>
</table>

Risk of HIV from a needlestick is 0.23% in the hospital setting
Blood-borne Viruses: Survival in the Environment

- HBV, HCV and HIV can all survive outside the human body for several weeks
- Virus survival influenced by
  - virus titer
  - volume of blood
  - ambient temperature
  - exposure to sunlight and humidity
Blood-borne Viruses: Transmission in Community-acquired Needlesticks

• Risk of transmission from syringes discarded in community settings appears to be very low

• A review of the literature
  – Little data
  – No infections
Risk after an Unintentional Needlestick or Other Sharps Exposure in the Community

- **417 children described in 7 published reports**
  - Community-acquired exposures occurring in public outdoor places or by reaching into needle disposal boxes at home or in a hospital
  - In all cases, the HIV status of the source person was unknown except in 1 report
    - involved multiple percutaneous exposures with lancets among 21 children while playing with discarded needles in a playground.
    - Some of the lancets had been used multiple times to stick different children.
    - One of the children stuck with a lancet was known to be HIV infected before the incident, not receiving ARV therapy, and documented to have an HIV-1 plasma viral load of 5,250,000 copies/mL; the other 20 children were considered potentially exposed to HIV
  - Among 155 children offered nPEP, 149 accepted and initiated nPEP, and 93 completed their 28-day nPEP course
  - No seroconversions for HIV, HBV, or HCV
Comparison of Blood borne Pathogens

<table>
<thead>
<tr>
<th></th>
<th>HBV</th>
<th>HCV</th>
<th>HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of chronic infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in US population</td>
<td>0.5%</td>
<td>1.8%</td>
<td>0.3%</td>
</tr>
<tr>
<td>in high risk groups</td>
<td>1-20%</td>
<td>1-90%</td>
<td>1-20%</td>
</tr>
<tr>
<td>Seroconversion after percutaneous exposure</td>
<td>6-30%</td>
<td>1.8%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Postexposure prophylaxis available</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Vaccine-preventable</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
Management of Case

• Obtain blood for:
  - Baseline HBV, HIV and HCV status
  - If ARVs are being considered: CBC with differential, AST, ALT, alkaline phosphatase, BUN and creatinine

• Testing needles and syringes for viruses is not indicated
# HBV Prophylaxis

<table>
<thead>
<tr>
<th>Situation</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child known to be HBV antibody- or HBsAg-positive</td>
<td>No action required.</td>
</tr>
</tbody>
</table>
| Child has not been fully vaccinated against HBV                          | Test for anti-HBs antibody and HBsAg. If results are not available in 48 h:  
  - Give HBlG immediately (ideally within 48 h of injury; efficacy unknown if >7 days after injury). Dose=0.06 mL/kg intramuscularly.  
  - Give HBV vaccine (as soon as possible, and at latest within 7 days of injury)  
  - If anti-HBs antibody- and HBsAg-negative, complete vaccine series  
  - If anti-HBs- or HBsAg-positive, discontinue vaccine series. Arrange appropriate follow-up if HBsAg-positive. |
| Child has been fully vaccinated against HBV                              | Test for anti-HBs antibody. If results are not available in 48 h, give dose of HBV vaccine.  
  If anti-HBs antibody-positive, no further action required.  
  If anti-HBs antibody-negative, test for HBsAg:  
  - If HBsAg-negative give HBlG and dose of HBV vaccine.  
  - If HBsAg-positive, arrange appropriate follow-up. |
Decision on HIV Prophylaxis

- Assess on a case-by-case basis
  - Risk of HIV transmission
  - Risks and benefits of ARV prophylaxis
- Take into consideration the ability of the child to tolerate and adhere to an ARV regimen for 4 weeks
- Discuss with parents and with the child, if age appropriate, the potential benefits, adverse effects and costs of ARV prophylaxis
HIV Prophylaxis

• ARV prophylaxis should be recommended only in cases of high risk
  – source is considered likely to have HIV
  – incident involved a needle and syringe with visible blood
  – blood may have been injected
HIV Prophylaxis

• In situations of low risk prophylaxis should not be recommended but should be considered
  – source unlikely to have HIV
  – no visible blood in the device
  – superficial injury
• Parents should be reassured of the low probability of their child acquiring HIV as a result of the incident
HIV Prophylaxis

• If the decision is made to begin ARV prophylaxis:
  – ARVs should be started as soon as possible, ideally within 1 h to 4 h of the injury
  – Prophylaxis is not recommended if not initiated within 72 h of the injury
• If parents considering prophylaxis are undecided, they should be advised that it is preferable to start prophylaxis immediately and then discontinue if they wish because starting later may be of no benefit
HIV Prophylaxis

- ARVs used should be those currently recommended for occupational and nonoccupational exposures
- Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV—United States, 2016 from the Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. 
HIV Prophylaxis

• ARVs are expensive
  • families may be unable to cover the out-of-pocket costs
• When insurance coverage is unavailable
  • Medication assistance programs available through the companies that manufacture the prescribed medications
    • applications available online that can be faxed to the company
    • certain companies can be called on an established phone line
  • Requests for assistance often handled urgently so that accessing medication is not delayed
• Information for specific medications and manufacturers is available
  https://www.pparx.org/prescription_assistance_programs/list_of_participating_programs
Preferred and Alternative Antiretroviral Medication 28-day Regimens for nPEP

<table>
<thead>
<tr>
<th>Age group</th>
<th>Preferred/ alternative</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescents aged ≥ 13 years, including pregnant women</td>
<td>Preferred</td>
<td>A 3-drug regimen consisting of tenofovir DF 300 mg <em>and</em> fixed dose combination emtricitabine 200 mg (Truvada) once daily <em>with</em> raltegravir 400 mg twice daily <em>or</em> dolutegravir 50 mg once daily</td>
</tr>
<tr>
<td></td>
<td>Alternative</td>
<td>A 3-drug regimen consisting of tenofovir DF 300 mg <em>and</em> fixed dose combination emtricitabine 200 mg (Truvada) once daily <em>with</em> darunavir 800 mg (as 2, 400-mg tablets) once daily <em>and</em> ritonavir 100 mg once daily</td>
</tr>
</tbody>
</table>
Preferred and Alternative Antiretroviral Medication 28-day Regimens for nPEP

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<thead>
<tr>
<th>Age group</th>
<th>Preferred/alternative</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children aged 2–12 years</td>
<td>Preferred</td>
<td>A 3-drug regimen consisting of tenofovir DF, emtricitabine, and raltegravir, with each drug dosed to age and weight</td>
</tr>
<tr>
<td>Alternative</td>
<td>A 3-drug regimen consisting of zidovudine and lamivudine with raltegravir or lopinavir/ritonavir, with raltegravir and lopinavir/ritonavir dosed to age and weight</td>
<td></td>
</tr>
<tr>
<td>Alternative</td>
<td>A 3-drug regimen consisting of tenofovir DF and emtricitabine and lopinavir/ritonavir, with each drug dosed to age and weight</td>
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</tr>
</tbody>
</table>
Follow-up of Needlestick Exposure

• Arrange follow-up
  – monitoring of side-effects if on ARV prophylaxis
  – testing for acquisition of infection
  – completion of HBV vaccination

• If receiving ARV prophylaxis:
  – Reassess at 2 to 3 days, by phone or visit
  – Follow-up at 2, 4 and 6 weeks for CBC with diff, AST, ALT, BUN and creatinine
Recommended Schedule of Laboratory Evaluations of Source and Exposed Persons

<table>
<thead>
<tr>
<th>Test</th>
<th>Source</th>
<th>Exposed persons</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Baseline</td>
</tr>
<tr>
<td>HIV Ag/Ab testing(^a) (or antibody testing if Ag/Ab test unavailable)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Hepatitis B serology, including:</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>hepatitis B surface antigen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hepatitis B surface antibody</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hepatitis B core antibody</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis C antibody test</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

\(^a\) Any positive or indeterminate HIV antibody test should undergo confirmatory testing of HIV infection status.
\(^b\) Only if hepatitis C infection was acquired during the original exposure; delayed HIV seroconversion has been seen in persons who simultaneously acquire HIV and hepatitis C infection.
\(^c\) If exposed person susceptible to hepatitis B at baseline.
\(^d\) If exposed person susceptible to hepatitis C at baseline.
Follow-up

- **At 4 weeks**, give second HBV vaccine dose if only one previous dose received or if no antibody or antigen detected on initial testing

- **At 6 months**, give third HBV vaccine dose if only two previous doses received
Follow-up

• If anti-HBs antibody negative at 6 months, test again one to two months after the third dose of vaccine
  – If still negative, test for HBsAg.
  – If negative for both, give a fourth dose of HBV vaccine and test again one to two months later.
  – If still negative, refer to an appropriate specialist
Follow-up

- If HIV, HCV or HBV infection occurs
  - test the stored baseline sera to determine whether infection was subsequent to the injury
  - arrange for appropriate follow-up
References

- Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV—United States, 2016 from the Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. 
References


Changes You May Wish to Make in Practice

1. Use LAIV for children only if child or family will not accept IIV
2. Consider adding an oral antibiotic when I&Ding a small skin abscess
3. Do not treat MRSA in children with non-purulent cellulitis
4. Screen and treat children with needle stick injuries appropriately for HIV, HBV and HCV
THANK YOU
Questions