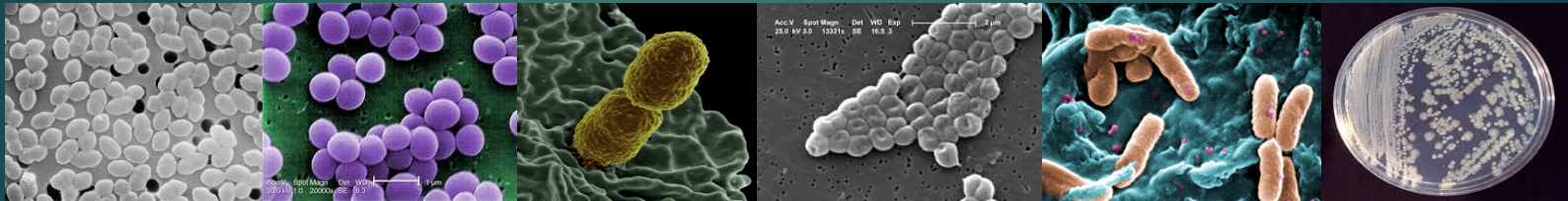


Infectious Diseases and Spinal Cord Injury



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My Patient Care Experience with Infections and SCI

- ▶ SCI Staff Physician at VA Puget Sound since 1996, and member of hospital's Infection Control Committee
- ▶ Changes in care during my career have included:
 - ▶ Recommendations for vaccinations against respiratory infections
 - ▶ Contact precautions for inpatients with resistant bacteria such as MRSA
 - ▶ Diagnosis and treating of osteomyelitis (bone infections) occurring with pressure injuries

My Research Experience with Infections and SCI

- ▶ Pneumonia
- ▶ Bloodstream infections
- ▶ Clostridium difficile (C diff)
- ▶ UTI's: antibiotics to prevent? And bladder colonization vs. UTI (with Dr. Felicia Skelton)
- ▶ Vital sign changes with severe infections (sepsis) – ongoing research with Dr. Shawn Song)

Outline

- ▶ Causes of infections
- ▶ Body's response to infections
- ▶ Effects of SCI on the immune system (my opinion)
- ▶ How the health care system deals with antibiotic resistance and control of infections
- ▶ Info on specific infections
- ▶ Prevention

Infectious Diseases as a Cause of Death following SCI

- ▶ “Infective and parasitic diseases” is the 1st or 2nd most common cause of death for people with SCI
- ▶ 28% of all deaths (versus only 5% of deaths in general population)
- ▶ A person with SCI is 35x more likely to die of pneumonia and 64x more likely to die of sepsis

Infection

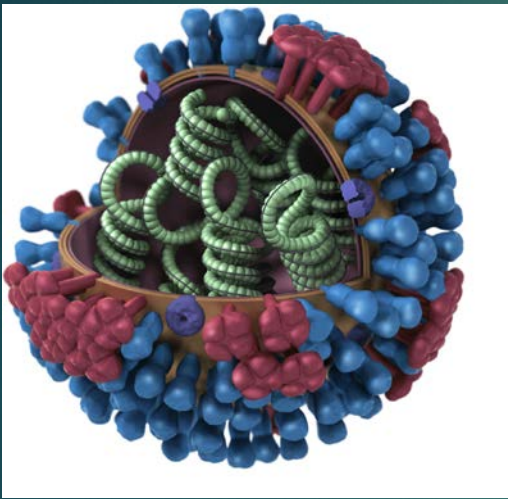
- ▶ **Infection** is the invasion of an organism's body tissues by disease-causing agents, their multiplication, and the reaction of host tissues to the infectious agents and the toxins they produce

- ▶ Note: agent has to be invading the tissue. Presence of bacteria on a body surface (skin, mouth, intestine, or even bladder) isn't necessarily infection.

Types of Living Organisms that cause Infectious Diseases (pathogens...GERMS!)

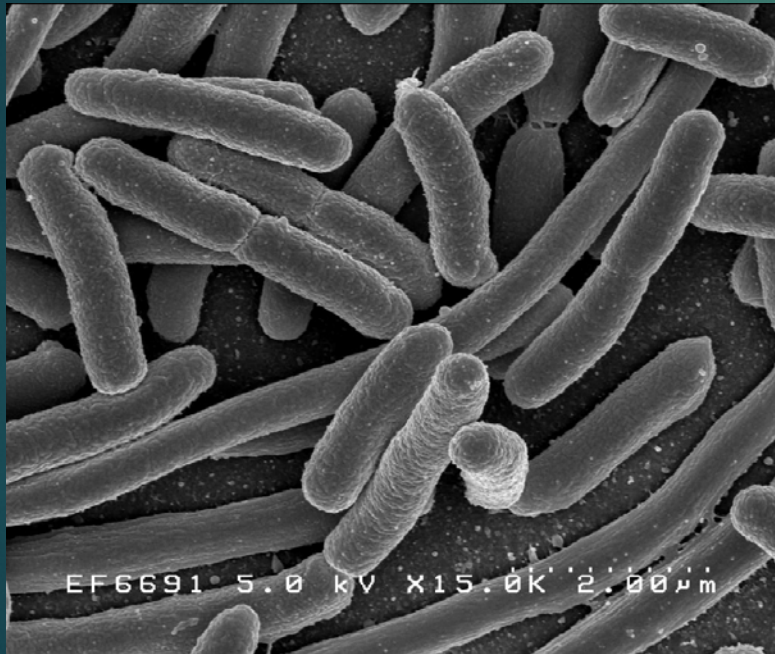
- ▶ * Viruses
- ▶ *** Bacteria
- ▶ Fungi
- ▶ Parasites: protozoa and worms

Viruses



- ▶ Small infectious agents that replicates only inside the living cells of other organisms.
- ▶ Most common virus of importance for people with SCI: influenza A (pictured here)
- ▶ Other viruses
 - ▶ Rhinoviruses (upper respiratory infections – “common cold”)
 - ▶ Hepatitis A, B, C

Bacteria



- ▶ Single-celled organisms found throughout the environment, on body surfaces, and through the digestive system.
- ▶ “Pathogenic bacteria” are the ones that can cause disease (infection).

Ways that Infections Develop

- ▶ Contact or airborne transmission of highly contagious infection from an infected to an uninfected person.
 - ▶ Influenza: cough, sneeze, snot from infected person touches another person's mouth, nose, or eye
 - ▶ Another example: infectious diarrhea
- ▶ Normal bacteria in mouth and nose move down through airway to enter the lungs, multiply, and cause pneumonia
 - ▶ This is more likely to occur if part of the lung isn't fully inflated, or if there are excessive retained secretions due to viral bronchitis

Ways that Infections Develop

- ▶ Direct entry of bacteria through an opening in the skin, allowing them to multiply inside the body tissue
 - ▶ Infection inside the skin: cellulitis
 - ▶ Infection of bone at base of pressure ulcer: osteomyelitis
- ▶ If infection is “inside the body tissue” it can also enter the blood
 - ▶ Infection in blood can go elsewhere in the body and cause infection at another site.
 - ▶ Bloodstream infections are serious and need stronger treatment

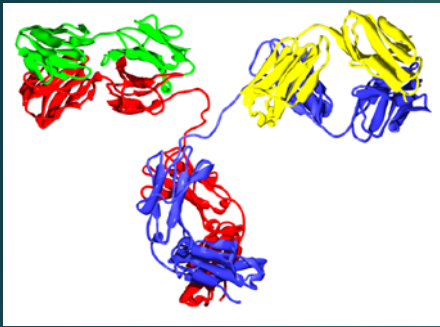
Infection:

Body Response and Treatment

- ▶ Body response
 - ▶ Specific immune system actions (antibodies, white blood cells)
 - ▶ Generalized inflammatory response and sepsis
- ▶ Treatment by health care providers
 - ▶ Drainage or removal of infected tissue (if required)
 - ▶ Antibiotics

Immune System Response

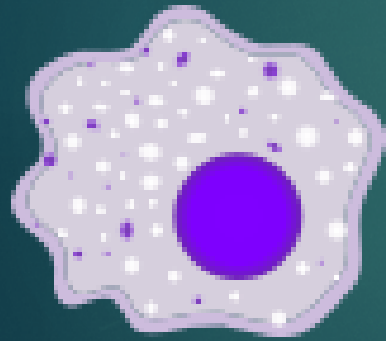
- ▶ Immune system function



- ▶ Antibodies: proteins produced by plasma cells (white blood cells) that inactivate microbes or “tag” them for destruction

- ▶ Macrophages (“big eaters”): white blood cells that engulf and digest microbes, dead cells, etc.

- ▶ A normal immune system prevents many microbes from ever causing disease.



- ▶ When the immune system is severely damaged (after chemotherapy; AIDS), bacteria and viruses that normally don’t cause illness can become harmful: “opportunistic infections.”

Immune Response Following SCI



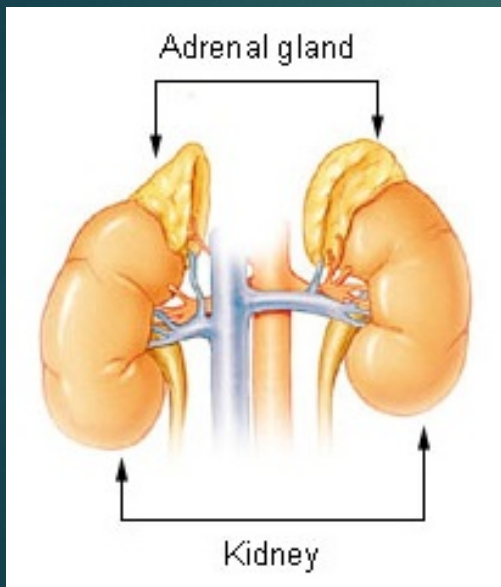
- ▶ No evidence that SCI causes any major and important change in the function of the immune system's antibodies and white blood cells
 - ▶ Some research shows minor changes in how white blood cells function
- ▶ Response to vaccines is normal
 - ▶ Vaccination = injection of material that stimulates production of antibodies that will attack a specific microbe
 - ▶ People with SCI don't need special versions of vaccine or higher doses

Immune Response Following SCI

- ▶ Individuals with SCI don't commonly develop "unusual infections" such as:
 - ▶ Atypical bacteria and viruses causing infections
 - ▶ Unexplained infections in unusual body locations
 - ▶ Or any "...only happens in people with SCI..." conditions
- ▶ **Bottom line:** frequent infections and death from infections are probably more common because of specific causative factors (catheter in bladder; retained lung secretions; deep pressure injuries), not because of immune system dysfunction

Reaction of Body to Infection

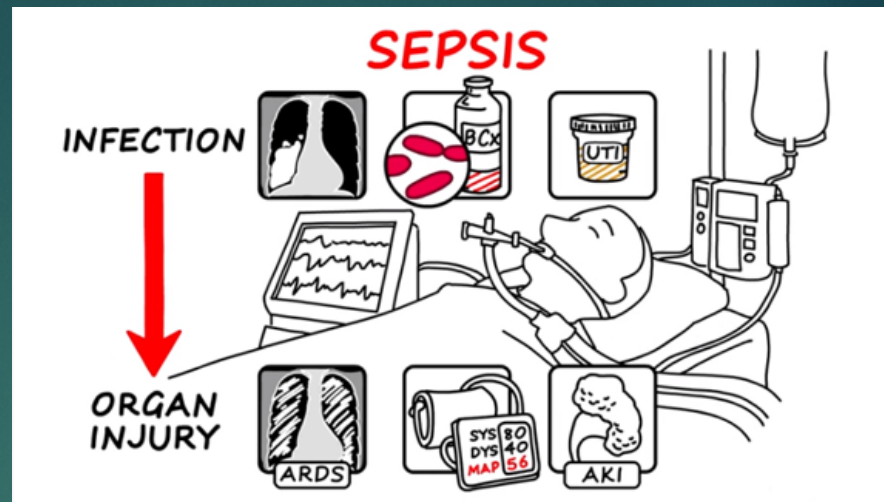
- ▶ Adrenal gland dysfunction could be a contributing factor in some deaths
 - ▶ Not uncommon to have “subclinical adrenal insufficiency” (steroids produced by the body when under stress) which could interfere with body’s response to stress such as sepsis
- ▶ However, when bloodstream infections occur in individuals with SCI, there is a lower rate of death than in general population



Inflammatory Responses of the Body to Infection

- ▶ Fever:
 - ▶ common and normal response to infection (or non-infectious conditions)
- ▶ Systemic Inflammatory Response Syndrome (SIRS): presence of at least 2 of these conditions –
 - ▶ Temperature greater than 100.4 (or less than 96.8)
 - ▶ Heart rate greater than 90 beats per minute
 - ▶ Breathing rate greater than 20 per minute
 - ▶ White blood cell count greater than 12,000 (or less than 4000)
- ▶ Can indicate severe illness due to infection, but also seen if body is successfully fighting infection

Sepsis



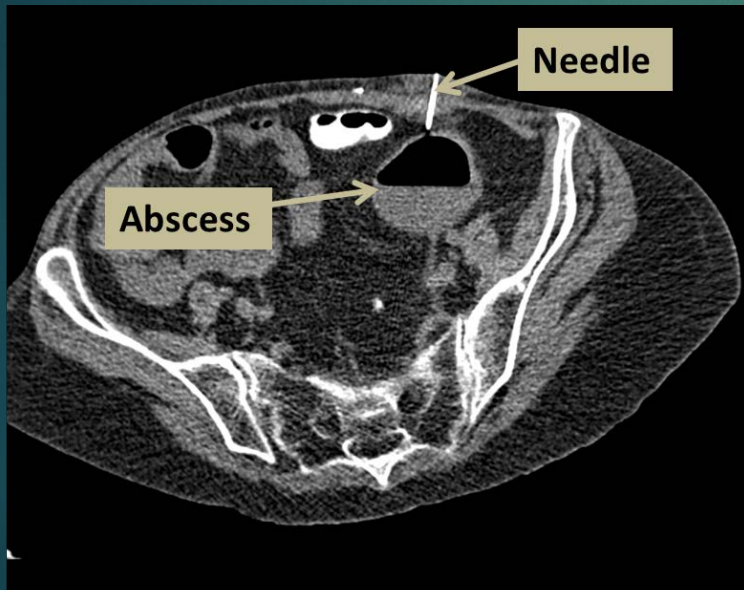
- ▶ **Sepsis** is a life-threatening condition that arises when the body's response to infection causes injury to its own tissues and organs
 - ▶ **Severe sepsis** is sepsis causing poor organ function, such as:
 - ▶ Lung injury (acute respiratory distress syndrome)
 - ▶ Kidney damage (acute kidney injury)
- ▶ **Septic shock** is low blood pressure due to sepsis that does not improve after reasonable amounts of intravenous fluids are given

SCI and Detection of Sepsis

- ▶ Guidelines for detection of sepsis use different combinations of vital signs and lab tests
- ▶ Recommended screenings include pulse, blood pressure, or temperature
- ▶ Preliminary data from a quality assurance project at Seattle VA show patients with sepsis who have tetraplegia (quadriplegia), as compared with paraplegia, have:
 - ▶ Less elevation of body temperature
 - ▶ Less elevation of pulse
 - ▶ (maybe) lower blood pressure
- ▶ May need different cutoff values for screening people with SCI



How is infection removed from the body? PROCEDURES



CT guided needle entering an abscess in the abdomen.

- ▶ Drainage or removal of infected tissue or abscess
 - ▶ If the infection is walled off inside the body (abscess) or within bone (osteomyelitis) and receives minimal blood flow, antibiotics don't reach the infection.
 - ▶ Simply opening and draining an abscess out to the skin can be all that's needed to stop sepsis and allow the immune system to clear the infection

How is infection removed from the body? MEDICATIONS

- ▶ Antimicrobial Medication: something that kills or stops growth of microorganisms
 - ▶ Antibiotic = antimicrobial that treats bacteria
 - ▶ Which antibiotic? Depends on the bacteria. Some are sensitive to many antibiotics, but some are resistant to nearly all.
 - ▶ Even when antimicrobials are used, most of the work to remove infection is done by the immune system



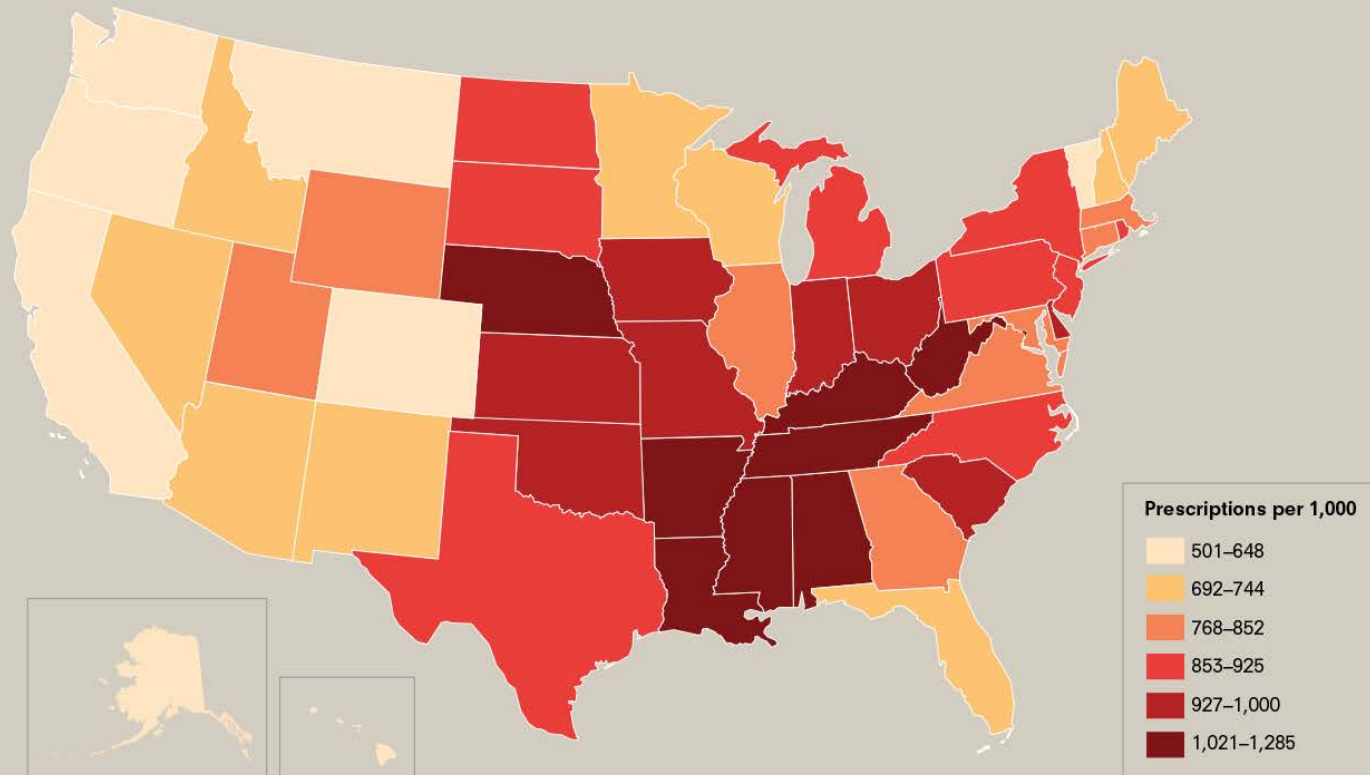
Antibiotics: Prescription, Resistance, and Stewardship



Over-prescribing of Antibiotics

Community Antibiotic Prescriptions per 1,000 Population by State — 2014

At least 30% of antibiotics prescribed in doctors' offices, emergency departments and hospital clinics are unnecessary.*



Data source: IMS Health Xponent 2014.

*Fleming-Dutra, K., et al. (2016). "Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011." *JAMA: the Journal of the American Medical Association* 315(17): 1864-1873.

Bacterial resistance to antibiotics

- ▶ When antibiotic therapy was first used in the early 20th century, most bacteria were sensitive to them
- ▶ Bacteria rapidly evolved resistance to antibiotics:
 - ▶ “Natural selection”: when antibiotics are used to treat an infection, all the sensitive bacteria are killed, leaving any that happen to be more resistant
 - ▶ Antibiotic-resistance genes can be exchanged between different species of bacteria
- ▶ Examples of bacteria with antibiotic resistance:
 - ▶ MRSA: methicillin-resistant *Staph. aureus*
 - ▶ Carried by about 20% of people with SCI vs. 2% of general population and 10% of hospitalized general population
 - ▶ VRE: vancomycin-resistant *enterococcus*

Risks of Antibiotics

Main considerations:

- ▶ Promotes drug resistance
 - ▶ People frequently treated with antibiotics are more likely to have highly resistant bacteria
- ▶ Antibiotic-associated diarrhea
 - ▶ Or super-infection by C diff (covered later)

Risks are greatest with

- ▶ Longer number of days of treatment
- ▶ Broader spectrum (stronger) antibiotics.

Antibiotic Stewardship



- ▶ Definition: Policies and interventions to improve antibiotic use by promoting the selection of the optimal drug, dosing, and duration of use
 - ▶ Goals include preventing bacterial resistance, reducing other side effects, and reducing cost.
- ▶ Components:
 - ▶ Hospital-specific treatment recommendations based on resistance patterns seen locally (antibiogram)
 - ▶ Reassessment of antibiotic choice after 48 hours
 - ▶ Restriction on use of certain antibiotics based on spectrum of activity
 - ▶ Audits and feedback to health care providers

How Providers Choose Antibiotics



1. Guess
2. Wild guess
3. Educated guess

Antibiogram: data for a hospital

Hospital XXX <u>Antibiogram</u>										
		% of n isolates susceptible to each antibiotic listed								
Bacteria	Number of isolates tested (n)	TOB	CFP	CTZ	PTZ	IMI	CIP	OXA	VAN	DAP
<i>E. cloacae</i>	192	65	77	66	79	96	85			
<i>E. coli</i>	1462	86	94	90	90	99	65			
<i>K. pneumoniae</i>	379*	78	80	79	86	97	81			
<i>A. baumannii</i>	117	63	61	57	69	73	66			
<i>P. aeruginosa</i>	928	65	73	71	88	76	44			
<i>S. aureus</i>	1178						44	41	100‡	100
<i>E. faecalis</i>	572								99	100
<i>E. faecium</i>	206								43	96

*20% of isolates are ESBL-positive
 ‡23% of isolates have vancomycin MIC = 2mcg/mL
 TOB = tobramycin; CFP = cefepime; CTZ = ceftazidime; PTZ = piperacillin/tazobactam; IMI = imipenem;
 CIP = ciprofloxacin; OXA = oxacillin; VAN = vancomycin; DAP = daptomycin
 Example adapted from Utilization of the Antibiogram in Clinical Practice accessed at
<http://www.bugsvsdrugs.com>

How Providers Choose Antibiotics



For some infections, cultures are sent to the lab

- ▶ Examples: urine, blood, sputum

Bacteria are grown in the lab and tested against different antibiotics

- ▶ "C+S": culture and sensitivity

Multi-Drug Resistant Organisms (MDRO)



- ▶ Risk factors (same for SCI as general population):
 - ▶ Amount of health care exposure
 - ▶ Prior antibiotics received
- ▶ Isolation Precautions: how hospitals try to limit the spread of MDRO or highly contagious infections
 - ▶ Standard precautions
 - ▶ **Contact precautions (most common for MDRO)**
 - ▶ Droplet precautions
 - ▶ Airborne precautions

Specific Infections

Urinary Tract Infections: Questions

- ▶ Difference between bacterial colonization and UTI
 - ▶ When to seek medical attention?
 - ▶ When are antibiotics needed?
 - ▶ Why do ER physicians think everyone with SCI has a UTI?

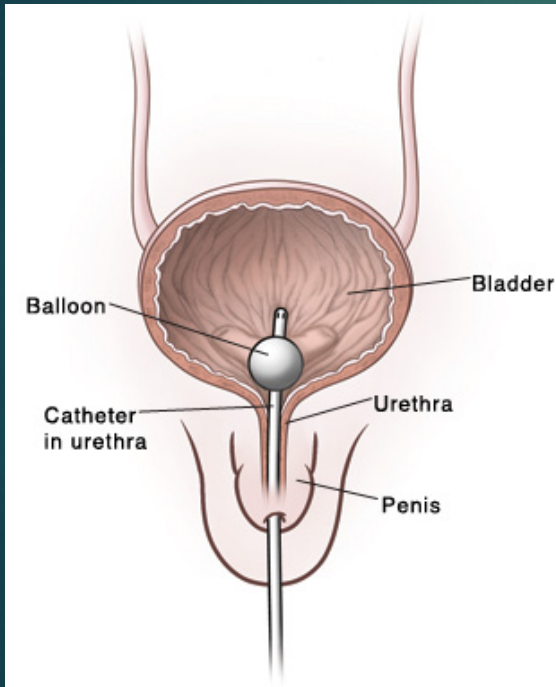
Urinary Tract Infections

- ▶ Normal urine in people without bladder dysfunction has a low concentration of bacteria (but is not sterile)
 - ▶ If a high concentration of bacteria is detected ($>100,000$ bacteria per cubic milliliter), it's usually because of urinary tract infection
- ▶ In people who use catheters, a high concentration of bacteria can be present without causing any signs and symptoms of infection: colonization (or "asymptomatic bacteriuria")
 - ▶ Change of appearance or smell of urine without other symptoms may mean that a new bacteria has colonized the bladder.



Urinary Tract Infections

- ▶ Bacteria in bladder can become symptomatic if they invade the bladder wall or travel backwards to the kidneys:



- ▶ Catheter blockage: stretches bladder or makes urine back up to kidney.
- ▶ Catheter trauma: scraping lining of bladder or ureter.
- ▶ “Host factors” that allow specific species of bacteria to invade host tissues

Challenge in SCI: UTI vs. Colonization

- ▶ Can't diagnose a UTI solely by urine tests results
 - ▶ Urinalysis; microscopic exam of urine for bacteria and white blood cells
 - ▶ Urine culture and sensitivity
- ▶ Need to look for signs and symptoms of infection:
 - ▶ Fever, malaise, elevated white blood cell count in blood
 - ▶ Changes in spasticity, discomfort (if person has sensation), other...

Challenge in SCI: UTI vs. Colonization – what's new?

- ▶ Researchers at Hines VA, as well as a former UW Resident (Felicia Skelton) at the Houston VA, recently received grant funding from VA to study this problem.
- ▶ So when should a patient be treated?
 - ▶ Fever or elevated white blood cell count on blood testing: yes
 - ▶ However: Need to consider other sources of infection: don't want to miss something that needs treatment other than antibiotics for UTI
 - ▶ Otherwise: judgment call on whether symptoms (such as increased spasticity or malaise) may be due to UTI

Role for prophylactic (continuously prescribed) antibiotics to prevent UTI's?

- ▶ Most research does not support it
 - ▶ Concern about promoting antibiotic resistance
- ▶ New study of nitrofurantoin (Macrochantin)
 - ▶ When receiving antibiotic, fewer patients received treatment for UTI: 57% vs. 36% had at least one UTI over a one-year period.
 - ▶ No evidence of increased antibiotic resistance (other than resistance to nitrofurantoin)
 - ▶ Note: findings are suggestive of benefit, but not conclusive

What about Cranberry? (juice, tablets)



- ▶ Proposed mechanism of action:
 - ▶ Acidifies urine
 - ▶ Contains compounds (proanthocyanidins) that could prevent *E. coli* bacteria from sticking to the bladder lining
- ▶ What does research show?
 - ▶ Benefit in people with SCI has not been proven in multiple research studies
 - ▶ Benefit in different patient populations has also been questioned recently

Bacteria to Prevent UTI's?

Bacterial Interference

- ▶ Intentionally introducing bacteria to colonize the bladder and prevent other bacteria from causing UTI
 - ▶ Uses bacteria that are less likely to cause UTI and are sensitive to many antibiotics
 - ▶ Preliminary research looks favorable
 - ▶ Some problems getting the bacteria to “stick around” in the bladder

Urinary infections: what else besides bladder infections?

- ▶ Kidney infections (pyelonephritis)
 - ▶ More serious than bladder infection (cystitis)
 - ▶ Complications can include sepsis, abscess near the kidney, or permanent reduction in kidney's filtering function
 - ▶ Symptoms can be similar to UTI, plus flank or low back pain (if sensation), more likely to have fever and nausea
 - ▶ Often requires longer treatment with antibiotics than UTI

Urinary infections: what else besides bladder infections?

- ▶ Kidney and bladder stones
 - ▶ The stones are often caused by bacteria (especially *Proteus* species) breaking down a substance in the urine.
 - ▶ Stones are a source for recurrent UTI (because bacteria living inside stone won't be completely treated by antibiotics)
 - ▶ Often the exact same bacteria causes UTI again and again
 - ▶ Kidney stones can suddenly block urine flow, and can damage kidney if they become very large
 - ▶ Severe infection can rapidly develop, requiring a temporary drainage tube

Respiratory infection: Questions

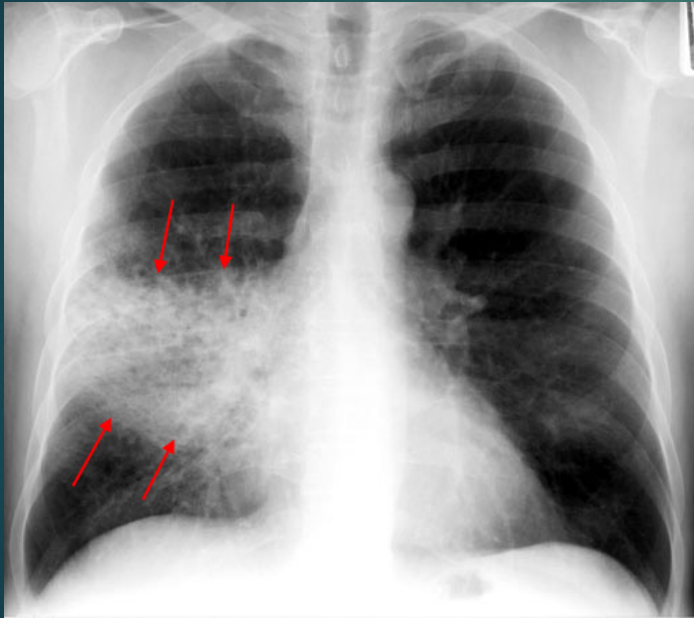
- ▶ When and how does a cold or cough become pneumonia?
- ▶ When should antibiotics be prescribed?

Respiratory Infections: Pneumonia



- ▶ Compared to general population:
 - ▶ “Increased incidence”: People with SCI are more likely to develop pneumonia
 - ▶ “Increased case-fatality rate”: If pneumonia occurs, it’s more likely to be fatal.
- ▶ Why is pneumonia common in people with SCI?
 - ▶ Weak expiratory muscles, causing ineffective cough and difficulty clearing secretions from lungs
 - ▶ Weak inspiratory muscles, causing poor expansion of lungs (atelectasis)
 - ▶ VA research shows pneumonia can follow episode of bronchitis: due to increased bronchial secretions?

When to be Concerned that Pneumonia has Developed, and How Pneumonia is Diagnosed

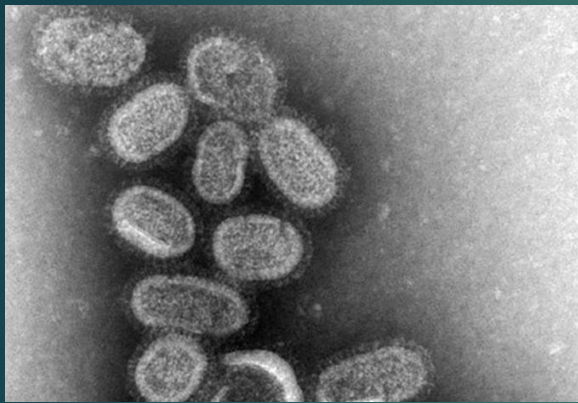


- ▶ Classic 3 symptoms: cough, fever, increased sputum (coughed-up secretions from lungs and bronchi)
- ▶ Oxygen saturation (on pulse ox) that stays lower than baseline and doesn't return to normal after clearing lung secretions: it's time to get evaluated
- ▶ Chest x-ray is often helpful in confirming diagnosis

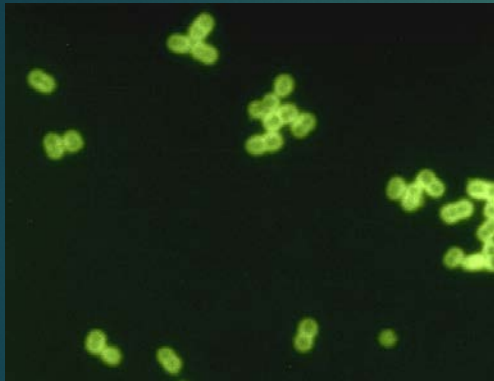
Immunizations to Prevent Respiratory Infections: Flu

▶ Influenza Vaccination

- ▶ Annual vaccination is recommended by CDC for all people with SCI, due to increased risk of death from respiratory infections.
 - ▶ When flu is fatal, it's often due to bacterial pneumonia that develops after flu begins
- ▶ SCI Service at VA Puget Sound typically achieves 75-80% vaccination rate for Veterans.



Immunizations to Prevent Respiratory Infections: Pneumococcal Pneumonia



- ▶ Vaccines to prevent pneumonia caused by *Streptococcus pneumoniae* (Pneumococcus), the most common bacterial cause of pneumonia in adults
- ▶ Not recommended by CDC for all people with SCI, but recommended by other organizations including VA.
- ▶ 2 different vaccine types; choice depends on age and which vaccine, if any, was previously received.

Bloodstream Infections and SCI



- ▶ When a primary infection source is identified, most common sources are:
 - ▶ urinary tract: more than 3/4
 - ▶ bone, skin, or wound
 - ▶ respiratory tract
- ▶ Rate is higher than seen in general population:
 - ▶ 7 per 100 hospital admissions
- ▶ When bloodstream infections occur in people with SCI, they are less likely to be fatal than when they happen in the general population.

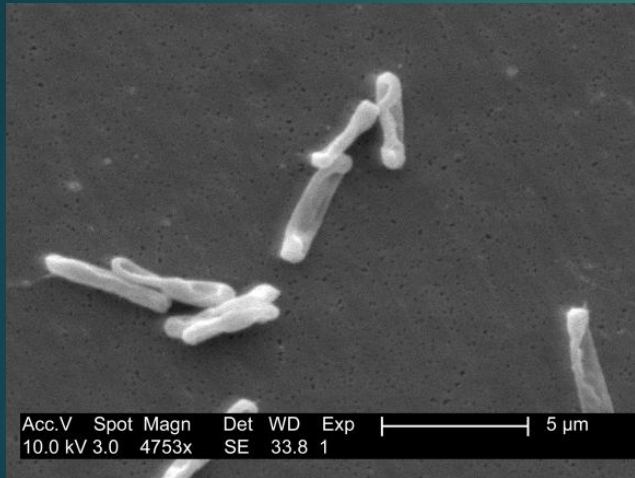
Skin, Soft Tissue, and Bone Infections

- ▶ Cellulitis: bacterial infection inside skin.
 - ▶ Treatment is similar to general population.
- ▶ Fournier Gangrene: necrotizing fasciitis of the groin and external genitals, beginning under the skin, caused by a mix of bacteria types, occurring primarily in males, with high rate of death
 - ▶ Rare infection, but more common (30x more common?) in people with SCI
 - ▶ Symptoms: swelling or pain in scrotum, fever, foul-smelling discharge from patches of skin that are dying
 - ▶ Treatment: surgical removal of dead skin; antibiotics

Skin, Soft Tissue, and Bone Infections

- ▶ Osteomyelitis at base of pressure ulcer
 - ▶ Common
 - ▶ Tests (MRI, bone scan) have limitations
 - ▶ Most antibiotics don't penetrate into bone very well, so the infected bone might need to be cut out with surgery
 - ▶ Our approach to osteomyelitis with pressure ulcers:
 - ▶ Preoperative antibiotics only if acute infection
 - ▶ Bone biopsy and culture at time of flap surgery
 - ▶ Post-op antibiotics based on culture results

Clostridium Difficile Infection (C Diff)



- ▶ Infection due to the spore-forming bacteria *Clostridium difficile*.
 - ▶ Causes C diff-associated diarrhea
 - ▶ More severe cases: sepsis; colon inflammation sometimes requiring surgery to remove colon.
- ▶ Primary risk factor is antibiotic use
- ▶ Treatment: more antibiotics
- ▶ Recurrences in up to 25% of patients after treatment antibiotic is stopped

C Diff and SCI

- ▶ Contamination of hospital environment with bacterial spores from an infected patient is an important cause of new infections
- ▶ Declining rate of C diff on VA SCI units between 2005 - 2010
 - ▶ Decreased from 13.5 to 7.5 cases per 10,000 hospital days
 - ▶ Possibly due to frequent use of contact precautions (mandatory gowns and gloves for patients with MDRO such as MRSA, on approximately 1/3 of patients) resulting in less movement of c diff spores from room to room
 - ▶ a “collateral benefit” from MRSA initiative

C Diff and SCI



- ▶ Risk factors for hospital-onset C diff:
 - ▶ Antibiotics: 30 times increased risk
 - ▶ Proton-pump inhibitors (reduce stomach acid production, to treat reflux): 8 times increased risk

What is different about C Diff in People with SCI?

- ▶ Possibly a longer time to regain (relative) stool continence
 - ▶ While in hospital, patients may remain on “enteric precautions” (might be confined to room) for longer than necessary while waiting to see if they have been adequately treated.
- ▶ No difference in rate of major complications like colon damage requiring surgery.
- ▶ Recent research: best choice of antibiotic to treat C diff may be different for people with SCI than for general population



Preventing Infections and Preventing Complications from Antibiotics

Questions: antibiotic prescription, antibiotic resistance

- ▶ What is overuse?
- ▶ Is it advisable to ride out an infection and hope that it passes without antibiotics?
- ▶ Can antibiotic side effects cause more problems than the infection?

Questions: what can be done to prevent infections?

- ▶ Can you bolster your immunity to infections?
 - ▶ Nothing conclusively proven to “boost immunity” other than vaccinations
 - ▶ So, make sure to receive all recommended vaccinations, especially for respiratory infections: pneumococcal vaccine, annual flu vaccine.
- ▶ Also, try to avoid unnecessary antibiotic treatment, to reduce the chance that a future infection will be resistant.
 - ▶ Realize that sometimes they are necessary (dental surgery; skin infections), and it’s a low chance that any one course of antibiotic treatment will cause lasting problems.
 - ▶ Educate your health care providers about UTI vs. colonization.

Preventing Infections



- ▶ Poor nutrition, not enough sleep, and other stresses on the body can affect the immune system, so try to avoid those factors
- ▶ If you have diabetes, follow management recommendations and avoid high blood sugars
 - ▶ Definite link between poorly controlled diabetes and increased risk of infections

Preventing specific infections

▶ Respiratory

- ▶ Flu and pneumococcal vaccinations
- ▶ Secretion mobilization (quad cough or CoughAssist; adequate fluids), as needed.
- ▶ Try to avoid viral respiratory infections (hand washing, etc.)

▶ Osteomyelitis

- ▶ Prevent pressure injuries to skin
- ▶ If an ulcer develops, initiate treatment to prevent it from deepening toward bone

Preventing specific infections

- ▶ Urinary tract infections
 - ▶ Follow provider's recommendations for your type of bladder management
 - ▶ Indwelling catheter:
 - ▶ change it on recommended schedule;
 - ▶ monitor for catheter blockage to prevent bladder overdistention
 - ▶ maintain adequate fluid intake and urine output as directed
 - ▶ Avoid tugging on catheter: tape it to thigh or use CathSecure

Preventing specific infections

▶ UTI's

- ▶ Intermittent catheter: cath frequently enough so bladder isn't overdistended
- ▶ Work with a knowledgeable provider so you understand your symptoms of UTI vs. bacterial colonization
- ▶ Receive period screening tests for kidney and bladder as recommended by your provider
 - ▶ Can detect kidney or bladder stones that cause infections

Preventing specific infections

- ▶ C diff
 - ▶ When possible, avoid receiving antibiotics
 - ▶ Discontinue medications that stop production of stomach acid (like Prilosec and Zantac) if they are no longer needed.
 - ▶ Or consider temporarily discontinuing while receiving antibiotics
 - ▶ Some evidence that probiotics (*Lactobacillus* (bacteria) and *Saccharomyces* (yeast) are helpful in preventing and treating C diff. Consider using when antibiotics are prescribed.

Summary: what's different about SCl, and why do we care?

- ▶ Infections are a more common cause of death than in the general population, and multi-drug resistant bacteria are common
- ▶ This occurs because of:
 - ▶ Altered function of body: bladder dysfunction and weak cough, for examples
 - ▶ Frequent exposure to antibiotics
 - ▶ Frequent contact with health care system
- ▶ Immune dysfunction is probably not a main contributing cause
- ▶ Urinary tract infections:
 - ▶ High rate of colonization, leading to misdiagnosis and unnecessary antibiotic treatment

Acknowledgments



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 - ▶ Info on antibiotic stewardship
 - ▶ Images of bacteria