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Neonatal sepsis and prevention of healthcare associated infections

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Jan Smíšek, MD.



Objectives

Neonatal sepsis

Drug Resistance

Prevention of Healthcare Associated Infections

Neonatal sepsis

- Bacterial
- Viral
- Fungal

Definition

In older medical literature, 1 week of age was considered the limit between EOS and LOS.

More recently, EOS infection is any infection that manifest in the first 72 hours, LOS manifest after 72 hours of birth

Source of Infection

EOS is usually due to vertical transmission by ascending contaminated amniotic fluid or during vaginal delivery from bacteria colonizing or infecting the mother's lower genital tract.

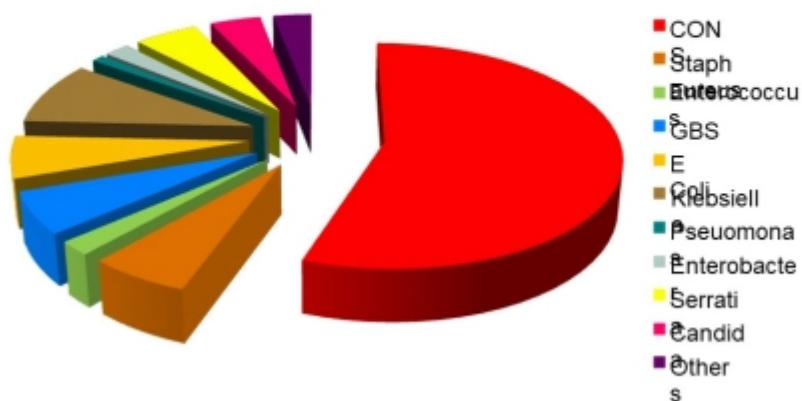
LOS can be vertical from the mother or horizontal transmission from direct contact with care providers or environmental sources.

Epidemiology

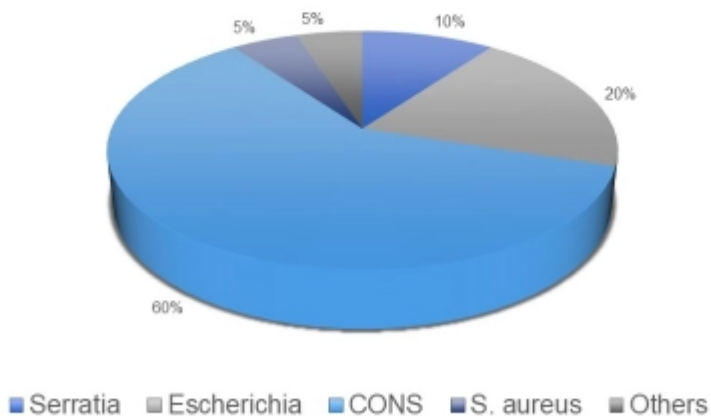
The overall incidence of neonatal sepsis ranges from 1 to 5 cases per 1000 live births.

- The estimated incidence is lower in term infants, with a reported rate of 1 to 2 cases per 1000 live births
- The incidence of early-onset sepsis has decreased primarily as a reduction of GBS infections due to the use of intrapartum antibiotic prophylaxis

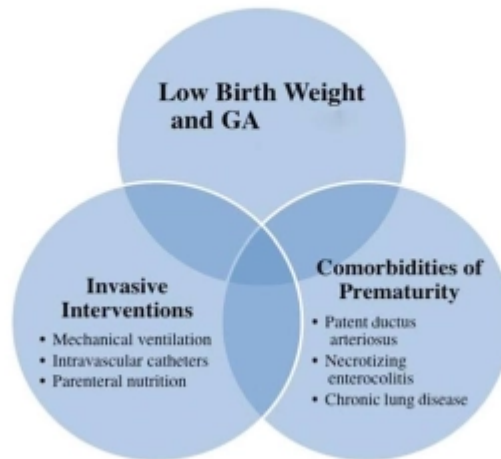
Epidemiology of LOS



Epidemiology of LOS GUH Prague



Risk factors for LOS



Risk factors for LOS

A recent study showed that empiric antibiotic treatment resulted in a threefold increase in risk of infection from resistant bacteria for every day of ampicillin and gentamicin use and up to a 34- fold increase with cephalosporin use in neonates previously exposed to antibiotics.

Clinical presentation

The primary clinical findings in a very low-birth weight infants

- Apnea (55%)
- Feeding intolerance, abdominal distension (43%)
- Increased respiratory support (29%)
- Lethargy and hypotonia (23%)

The most common clinical syndromes of early-onset disease are sepsis and pneumonia; less frequently meningitis. Late onset presents as sepsis and meningitis. The case-fatality ratio of early-onset disease has declined from as high as 50% in the 1970 to 3-4 % in Full term and 20% in preterm infant.

Diagnosis – blood culture

Positive blood culture is considered the gold standard in sepsis diagnosis.

- Positive results from blood culture depend on the technique used, microorganism density, previous antibiotic treatment, and sample volume.
- The automated method requires only 1.0 mL of blood and with the radiometric technique is very sensitive, with a high percentage of positive blood cultures, reaching 74% to 90.
- Blood culture should be collected by peripheral venipuncture before beginning antibiotic treatment, and if positive, should be repeated during treatment to evaluate treatment effect.
- Patients who have central catheters can have blood obtained by this route, but another sample should be collected by peripheral access for better interpretation of results.
- Positive blood culture confirms sepsis, and when the blood culture is negative, the condition is considered as clinical sepsis.
- An alarming fact in many neonatal intensive care units (NICUs) is that for each confirmed case of infection, between 11 and 23 uninfected newborns are treated.

Diagnosis – urine culture

Urine culture obtained by catheter or bladder tap should be included in the sepsis evaluation for infants >6 days of age.

A urine culture need not be routinely performed in the evaluation of an infant ≤ 6 days of age because a positive urine culture in this setting reflects high-grade bacteremia rather than an isolated urinary tract infection.

Diagnosis – CSF culture

The decision whether or when to perform a LP for CSF analysis and culture remains controversial.

As many as 25% of newborns who have sepsis have meningitis, and 15% to 55% of patients who have meningitis (positive CSF culture) have negative blood cultures.

The approach outlined by the 2012 AAP clinical report recommends that LP should be performed for an infant with any of the following clinical conditions

A positive blood culture

- Clinical findings that are highly suggestive of sepsis
- Laboratory data strongly suggestive of sepsis
- Worsening clinical status while on antibiotic therapy

Diagnosis – WBC

Total white count

Absolute neutrophil count

- Ratio of immature to total neutrophil counts (I/T ratio)
- Both are more useful in identifying
- Platelets count

Diagnosis – Cytokines, Acute phase reactants and Surface Markers

- IL 6 –IL 8 – IL 10
- Tumor necrosis factor alpha
- CD64
- CRP
- PCT

Diagnosis – CRP

C-reactive protein was the best single marker, with an

- overall sensitivity and specificity of 84% and 96%, respectively.

At the beginning of sepsis, CRP concentrations are increased (1 mg/dL) in only 16% of cases, After 24 hours, positivity increases to 92%.

Performing IL-6 and C-reactive protein on day 0, together with either TNF alpha on day 1 or C-reactive protein on day 2, showed the best overall sensitivity (98%) and specificity (91%) for the diagnosis of late onset infection.

CRP levels can be considered as a criterion for the discontinuation of antibiotic therapy to minimize antibiotic exposure and shorten hospital stay.

Diagnosis – Neutrophil CD64

Diagnostic Marker in Neonatal Sepsis.

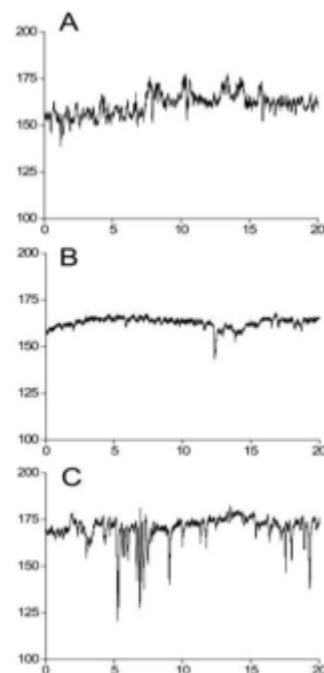
Can be incorporated as a valuable marker for excluding neonatal sepsis.

- A cut-point value, sensitivity, specificity and a negative predictive values of 3.62, 75%, 77%

Test	S%	SP%
Gram-specific PCR for Gram -ve	86	99
Gram-specific PCR for Gram +ve	74	98.5
Tumor necrosis factor -alpha	73-82	80-94
IL-6+CRP or PCT	100	96
IL-8+CRP	80	87
IL-8 urine	92	94
CD64+IL-6 or CRP	100	88

Diagnosis – Heart Rate Characteristics

A new technology related to heart rate characteristics (HRC) monitoring may be a promising tool in the early diagnosis of LOS 24 hours before clinical suggestions of sepsis, neonates have reduced heart rate variability and transient decelerations. Although the mechanism by which sepsis leads to these abnormalities is not known, it is speculated that cytokines play a role.



Diagnosis – Heart Rate Characteristics

Choice of antibiotic therapy for suspected sepsis should be tailored for the most likely organism with the highest mortality risk with consideration to local resistance patterns.

There is inadequate evidence from randomized trials in favor of any particular antimicrobial regimen for the empirical treatment especially for suspected LOS.

Treatment

Optimal duration of empiric antimicrobial use decreases the development of antimicrobial resistance, prevents unwanted changes in flora found in the NICU, and minimizes unnecessary expenses for infants who have negative blood culture

Prolonged duration of initial empirical antibiotic therapy is associated with adverse effects.

Vancomycin: CDC recommended against empirical vancomycin therapy to prevent the emergence and spread of vancomycin resistant strains and recommends its use in areas where MRSA is prevalent.

An acceptable approach would be to start with cloxacillin and gentamicin as initial antibiotics for LOS in a stable neonate.

Third generation cephalosporin: provides less coverage for the relevant disease-causing organism and increase resistance and risk for fungal infections.

This rule does not apply for meningitis.

10 days of therapy for culture-proven sepsis with minimal or absent focal infection.

Neonates with *S. aureus* infection may require 14 days of antibiotic therapy.

This applies to patients who are at least 32 weeks and above and showed good initial response to antibiotics.

For neonates with late-onset meningitis, a regimen containing an antistaphylococcal antibiotic, such plus cefotaxime or ceftazidime with or without an aminoglycoside is recommended.

GBS meningitis is usually treated for 14 to 21 days.

For meningitis caused by Gram-negative bacteria, a minimum of 21 days is recommended.

Avoid treating colonization and prophylactic antibiotic use for invasive devices

IVIG

The rationale for IVIG infusion is that it could provide type-specific antibodies

The main difficulties with IVIg therapy are as follows:

- The effect has been transient
- Clinically available IVIg solutions do not contain type-specific antibody
- The adverse effects associated with the infusion of any blood product can occur

Complication

Meningitis: hearing and vision impairment, convulsions, neurodevelopmental impairment, behavioral problems.

At school age, a majority of preterm children with late-onset sepsis had motor problems and lower IQ was and memory and attention were specifically impaired.

Healthcare associated infection

Multidrug resistant bacteria

**ESBL's history starts, as many histories do, with a war:
The war between us and the bacteria**

Penicillin

Beta

Lactamase



Cephalosporins



ESBL

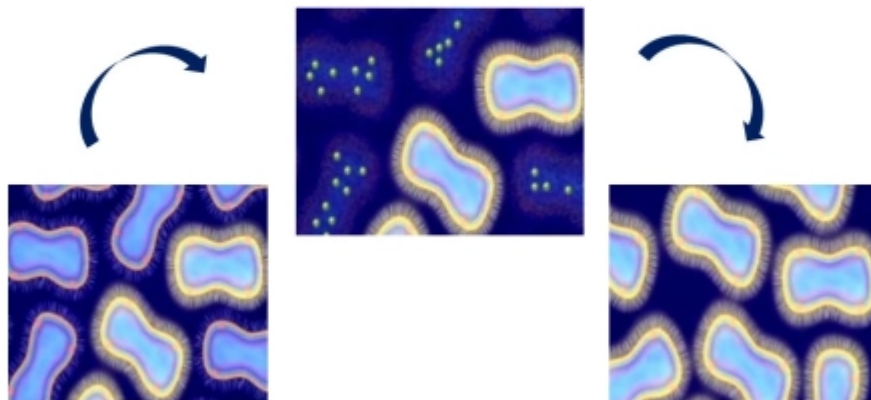
Carbapenems

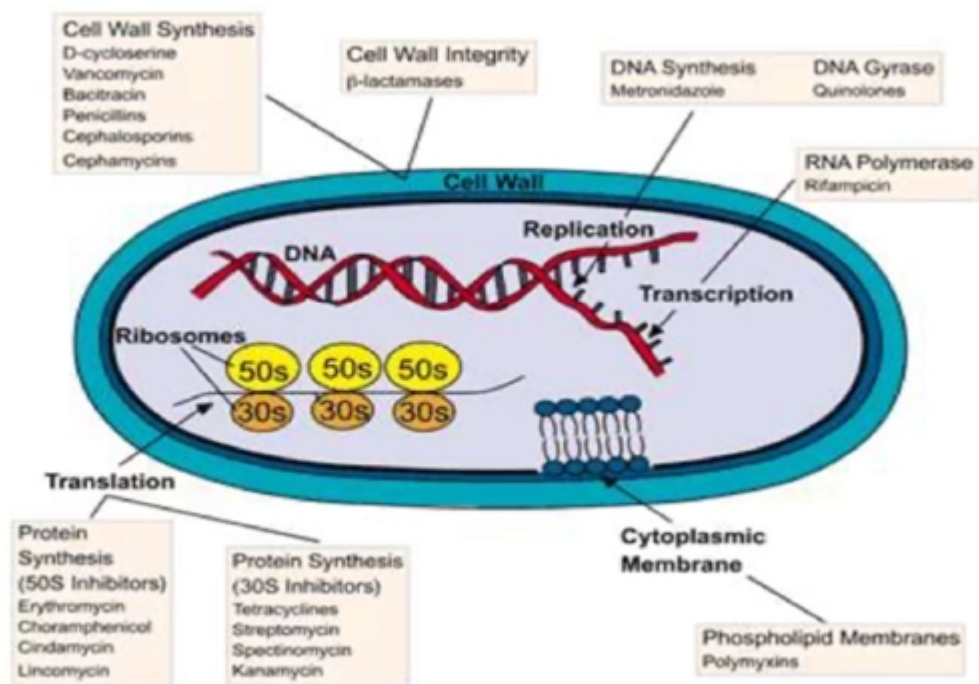
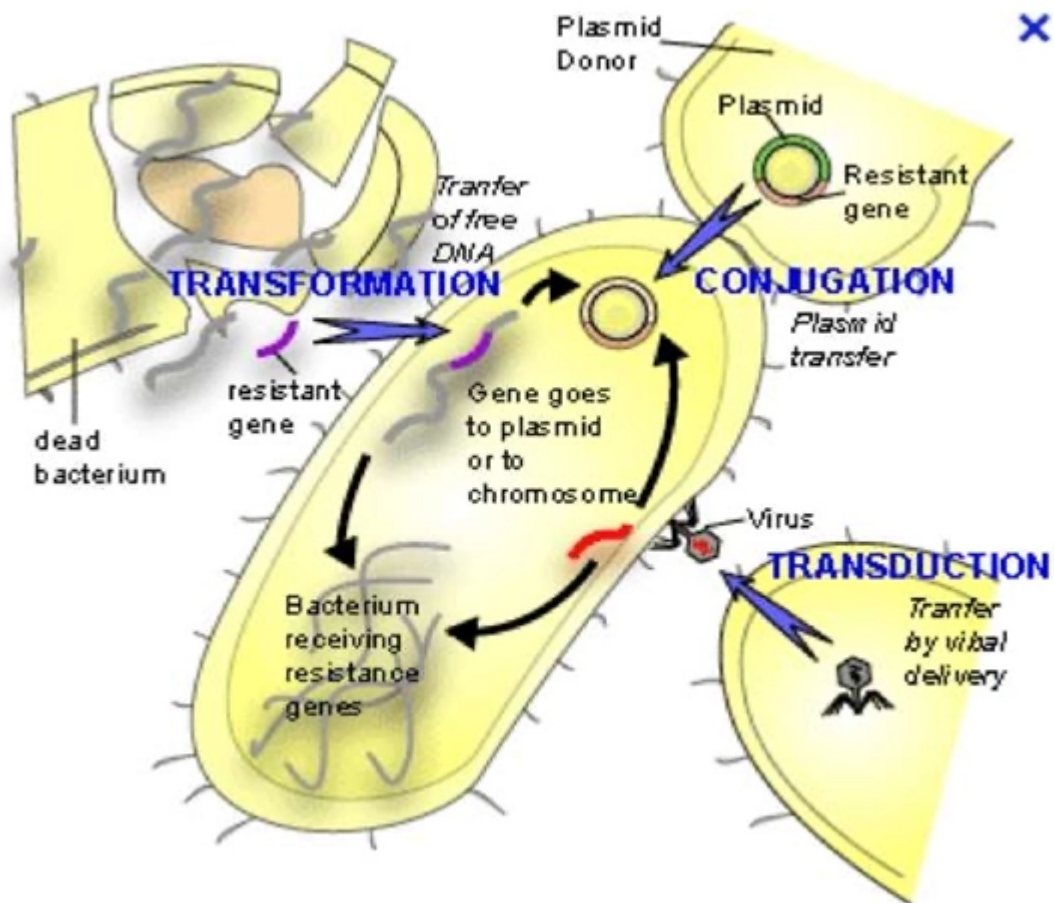


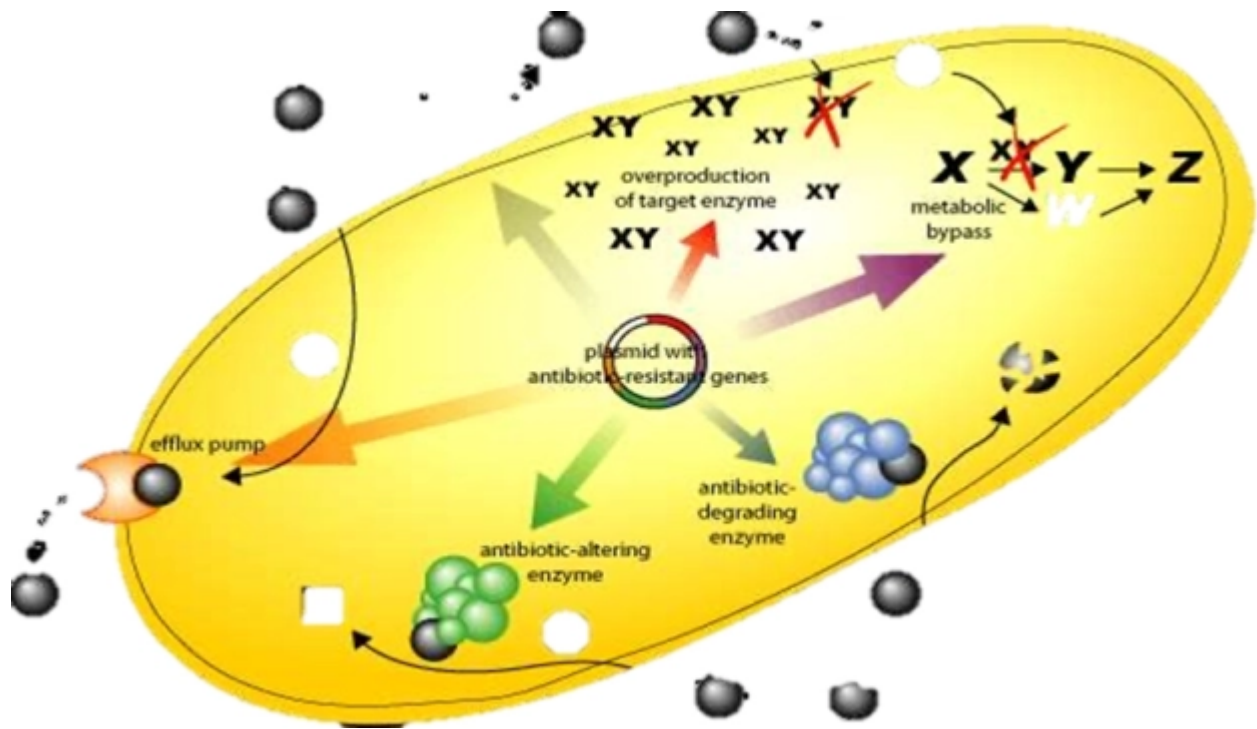
ESBL, NDM-1



Selection pressure
"Survival of the Fittest"







Definition

Nosocomial infection or Hospital acquired infection:

An infection occurring in a patient in a hospital or other healthcare facility in whom the infection was not present or incubating at the time of admission.

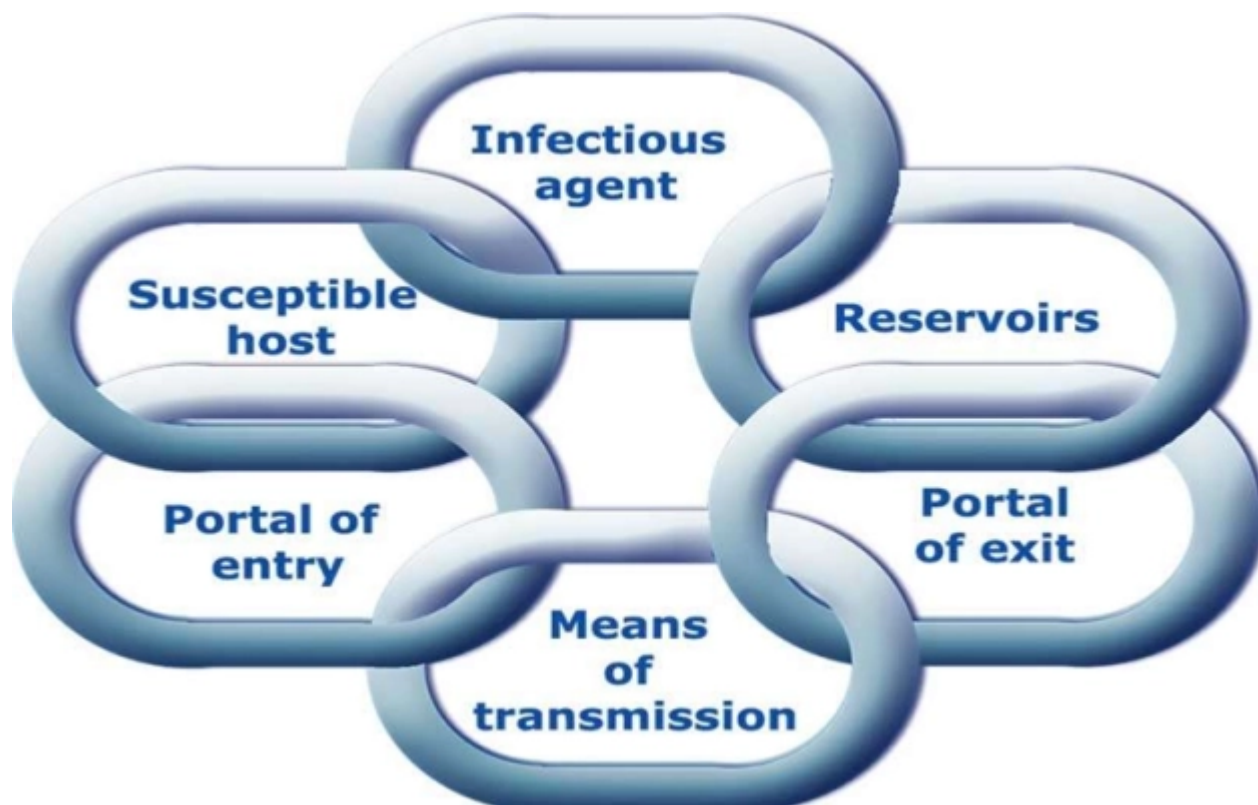
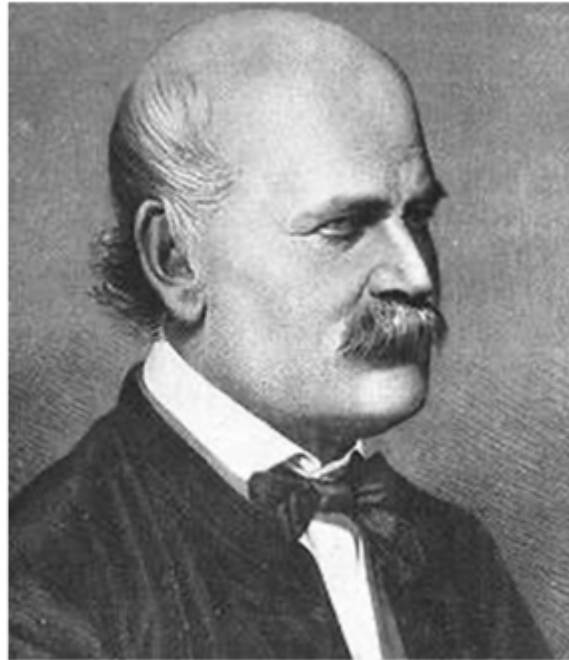
This includes infections acquired in the hospital but appearing after discharge.

Prevention

Ignaz Semmelweis

(1818 -1865)

- Hungarian obstetrician
- Pioneer of antiseptic procedures
- Decreased incidence puerperal fever and maternal mortality by 90%
- Hand hygiene



Prevention of HCAI

Validated and standardized prevention strategies have been shown to reduce HCAI.

At least 50% of HCAI could be prevented.

Most solutions are simple and not resource-demanding and can be implemented in developed, as well as in transitional and developing countries.

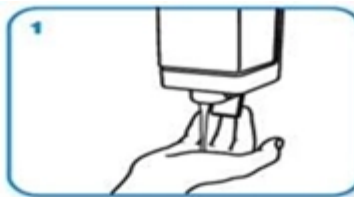
- Reducing person to person transmission
- Controlling environmental risks for infection
- Protecting patients with appropriate use of prophylactic antimicrobials, nutrition, and vaccinations
- Limiting the risk of endogenous infections by minimizing invasive procedures, and promoting optimal antimicrobial use
- Surveillance of infections, identifying and controlling outbreaks
- Prevention of infection in staff members
- Enhancing staff patient care practices, and continuing staff education

Clean Hands ... Save Lives





Wet hands with water



apply enough soap to cover all hand surfaces.



Rub hands palm to palm



right palm over left dorsum with interlaced fingers and vice versa



palm to palm with fingers interlaced



backs of fingers to opposing palms with fingers interlocked



rotational rubbing of left thumb clasped in right palm and vice versa



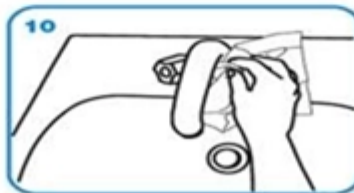
rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa.



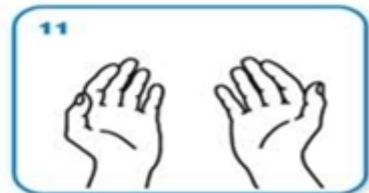
Rinse hands with water



dry thoroughly with a single



use towel to turn off faucet



...and your hands are safe.



Compliance with hand hygiene

Compliance with hand hygiene differs across facilities and countries, but is globally <40%

Main reasons for non-compliance reported by health-care workers:

- Too busy
- Skin irritation
- Glove use
- Don't think about it

Time constraint = major obstacle for hand hygiene

- Adequate handwashing with water and soap requires 40–60 seconds
- Average time usually adopted by health-care workers: <10 seconds
- Alcohol-based hand rubbing: 20–30 seconds