Hospital infection: from Semmelweis to molecular detection

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Hospital infection - definition

- An infection caught while hospitalized.
- The medical term for a hospital-acquired infection is "nosocomial."
- Most nosocomial infections are due to bacteria.
- Since antibiotics are frequently used within hospitals, the types of bacteria and their resistance to antibiotics is different than bacteria outside of the hospital.
- Nosocomial infections can be serious and difficult to treat.

Hospital infection - definition

- A nosocomial infection is strictly and specifically an infection "**not present or incubating prior to admittance to the hospital, but generally occurring 72 hours after admittance**.“
- The word "***nosocomial***" is made up of two Greek words. The prefix "***noso-***" comes from "***nosus***" meaning **disease** and "***-comial***" comes from "***komeion***" meaning **to take care of**.
- It now refers more narrowly to a hospital-acquired infection.

Hospital infection - definition

- “Hospital-acquired infection” means a localized or systemic condition:

(1) that results from adverse reaction to the presence of an infectious agent(s) or its toxin(s) and

(2) that was not present or incubating at the time of admission to the hospital.

Community-acquired infection

- Those infections that are acquired outside of health-care facilities

Iatrogenic infections

- *Iatrogenic*: “physician- induced”
- Are the result of medical or surgical treatment and are caused by surgeon, other physicians, or other health-care personnel.

Hospital infection – times, particularities and notions

- Times before Pasteur
- Pasteur’s times
- Antibiotics’ times

Times before Pasteur

- IVth century: Saint Basil of Caesarea: (BC 330-379) first hospitals and conditions for cross-infections.

St. Basil, detail of a mosaic, 12th century; in the Palatine Chapel, Palermo, Sicily, Italy. (credit: Alinari/Art Resource, New York)

XVIII Century

- Separated hospitals: general hospital and hospitals for febrile patients.
- No statistics arguments for this.

Oliver Wendell Holmes

- 1840, Oliver Wendell Holmes (1809 – 1894), Boston;
- He had concluded that puerperal fever was spread by healthcare workers' hands.
- 1843: published the essay entitled "*Contagiousness of Puerperal Fever*";
- His recommendations meet with opposition and had little impact.
- He initiate antiseptic measures to combat puerperal fever.

Ignaz Philipp Semmelweis
(1818 – 1865)

Ignaz Philipp Semmelweis

- **Ignaz Philipp Semmelweis**, also **Ignac Semmelweis** (born **Semmelweis Ignác Fülöp**), was an Austrian-Hungarian physician called the *"savior of mothers"* who discovered, by 1847 that incidence of puerperal fever could be decreased by using of hand washing standards in obstetrical clinics.
- I.P. **Semmelweis**, has been referred to as the “Father of Handwashing”, the “Father of Hand Disinfection”, and the “Father of Hospital Epidemiology”.

Ignaz Philipp Semmelweis

- Puerperal fever (*childbed fever*) was common in mid-19th century hospitals and often fatal, with mortality at 10%-35%.

- Semmelweis postulated the theory of washing with "chlorinated lime solutions“ in 1847 as head of Vienna General Hospital's First Obstetrical Clinic, where doctor wards had 3 times the mortality of midwife wards.

- In 1851, Semmelweis moved to work in Hungary, which accepted the theory by 1857.

Ignaz Philipp Semmelweis

- Despite his publications by 1861 of statistical trials where hand-washing reduced mortality below 1%, Semmelweis' practice only earned widespread acceptance years after his death, when **Louis Pasteur** confirmed the ***germ theory***.

Ignaz Philipp Semmelweis

- In the mid-19th century it was common for a doctor to move directly from one patient to the next without washing his hands, or to move from performing an autopsy on a diseased body to examining a living person.
- Semmelweis hypothesized that "particles" introduced into the women caused puerperal fever, and that these particles were spread on the hands of the doctors and students.

- **Semmelweis ordered that hands be washed in a chlorine solution before each examination.**

Ignaz Philipp Semmelweis

Ignaz Philipp Semmelweis

- Mortality rates among women attended by doctors and medical students quickly dropped from 18 to 1percent.
- In 1861, Semmelweis published a book that described his findings and recommendations.
- He influenced **Joseph Lister** but years passed before the importance of disinfection was widely appreciated.

Florence Nightingale (1820-1910) The founder of modern nursing

- 1863: her experience from Crimean war was the support of *“Notes on Hospital”*

Florence Nightingale

- 1853 – superintendent of the Hospital of Invalid Gentlewomen – London.
- In 1854, she volunteered for service in the Crimean War: she assumed direction of all nursing operations at the war front and, as a results of her insistence on sanitary measures, the mortality rates among the sick and wounded were drastically reduced.

Florence Nightingale

- In **1860**, she founded the Nightingale School of Home for Nurses at St. Thomas's Hospital in London – the beginning of professional education in nursing.

Florence Nightingale

- In recognition of her hard work Queen Victoria awarded Miss Nightingale the Royal Red Cross in 1883.
- In her old age she received many honors, including the Order of Merit (1907), becoming the first woman to receive it.

1860

- Nosocomial infections' mortality reach 25-40% (children) to 60% (surgery, lying-in woman).

Louis Pasteur and "germ theory"

- Louis Pasteur demonstrated that the fermentation process is caused by the growth of **microorganisms,** and that the growth of microorganisms in nutrient broths is **not due** to **spontaneous generation**

  (held that complex, living organisms are generated by decaying organic sub-stances, e.g. that mice spontaneously appear in stored grain or maggots spontaneously appear in meat).

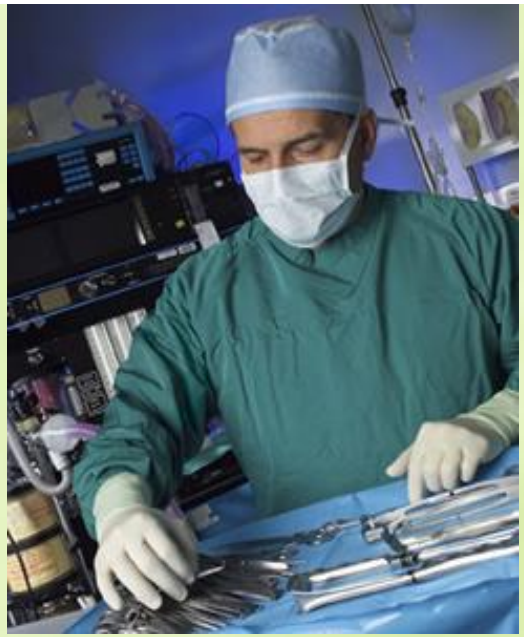
Joseph Lister (1827 – 1913)

- 1867: a British surgeon
- The inventor of antiseptic surgery

Joseph Lister

- He made significant contributions in the areas of antisepsis (“against infection”) and asepsis (”without infection”).
- During 1860s, he instituted the practice of using phenol (carbolic acid) as an antiseptic to reduce microbial contamination of open surgical wounds.

Joseph Lister



- Later contribution by Lister included such aseptic techniques as steam sterilization of surgical instruments: the use of sterile masks, gloves, and gowns by member of the surgical team; the use of sterile drapes and gauze sponges in the operating room.
- Lister's antiseptic and aseptic techniques greatly reduced the incidence of surgical wound infections and surgical mortality.

Von Bergman (1836 – 1907)

- 1894: aseptic surgery (steam sterilization of equipment).

clendening.kumc.edu/dc/pc/b.html

W.S. Halsted

- 1913 – surgical gloves

C. Dukes

- 1929 – catheter *ả demeur* and bladder infection: invasive procedure and acquired infection through exploratory procedures.

IInd World War

- 1939-1945: in war hospital conditions, the high incidence of open wounds infections shown a high risk for nosocomial infections.

Antibiotics era

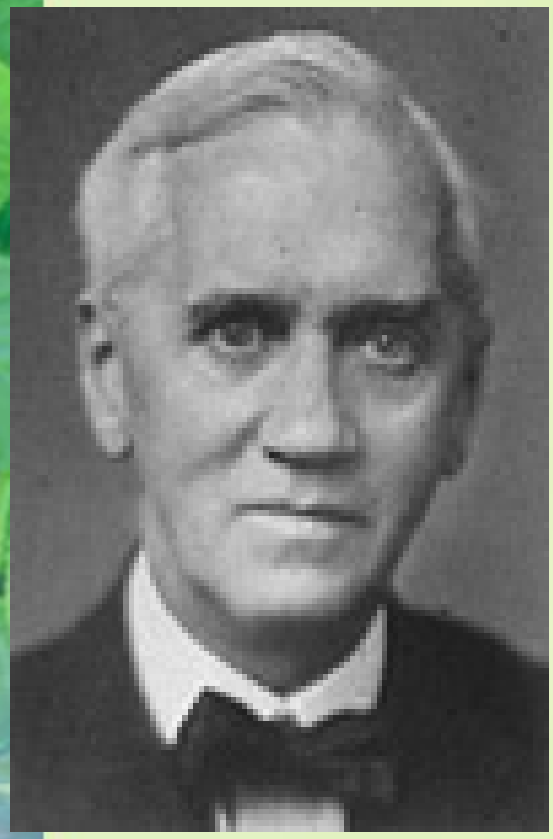
- Particularities:
- Antibiotics treatment changed the NI profile: *S. pyogenes* infections fallen.
- New therapeutically and diagnosis invasiveness methods were introduced on medical field in parallel with immuno-suppressive treatment (iatrogenic) or induced by HIV.

Gerhard Domagk – desoverer of sulphonamides

- 1932: demonstrated that «prontosil rubrum» (derivative of sulphanilamide, synthesized by Gelmo in 1908) protected mice and rabbits against lethal doses of staphylococci and haemolytic streptococci.

Gerhard Domagk

- 1939: Nobel Prize Medicine



Fleming, Chain and Florey –Nobel Prize Medicine, 1945

Penicillin - 1928

Salman Abraham Waksman

- 1943 –streptomycin
- 1952 - Nobel Prize Medicine

Tsutomu WATANABE

- 1963: demonstrated transferable antibiotic resistance – R factor

A new post-antibiotics times?

- Particularities
- Hospital infection will survive as long as hospitals are in place
- New bacteria strains resistant to all antibiotics
- New prevention program of NI in some countries
- Can we reduce the prevalence of NI until 0%?

A new post-antibiotics times?

- 1967: plasmides of commensale *Enterobacteriacae* are the main way of antibiotics resistance spread. Gram negative bacilli: the most frequent cause of NI.
- 1980: New bacteria reached the top: Gram positive cocci (oral streptococci and staphylococci – nonβ lactamase genes and multi-resistant strains).

Modern NI

- 1987, N.P.C. MOLAN: first outbreaks of *C. difficile* post-antibiotics psudomembranouse colitis.
- 1989, R.C. GEORGE: first epidemic NI (enterococci resistant to all antibiotics).
- 1990: F.W. GOLDSTEIN: meticilline resistant coagulase negative staphylococci (intermediate resistant to vancomycine.

Modern NI

- 1993, C.M. KUNIN
- 1994, A. TOMASZ - announced that the end of antibiotics era is near.
- Later 1992: the decrease of prevalence of NI as result of prevention programms.
- This is the last stop?

Pathogenesis of NI

- Major factors:
- susceptible host
- virulent organism
- portal (mode) of entry

Hospital as microorganisms reservoir

- **Human beings - patients, hospital staff** and **visitors** - represent the ***primary reservoir*** of normal human microbiota in the hospital.

Patients

- Host defenses depressed by underlying disease or treatment, malnutrition, age
- Anatomic barriers breached (IV's, foleys, vents etc.)
- Exposure to virulent pathogens
  - many resistant to multiple antibiotics

Hospital as microorganisms reservoir

- The ***secondary reservoirs*** of these microorganisms include **all environments** in which nutrients, humidity and temperature are adequate for their survival, such as hydrotherapy and dialysis equipment, equipment fitted with air humidifiers, nebulizers of all types, food kept at room temperature or at inappropriate temperatures, and others.

Hospital as microorganisms reservoir

- Although some of the pathogens that cause NI come from external environment, most come from the **patients themselves** – their own indigenous microflora that enter a surgical incision or otherwise gain entrance to the body.

Sources of microbes

- patient's own flora
- cross infection from medical personnel
- cross infection from patient to patient
- hospital environment- inanimate objects
  - air
  - Dust
  - IV fluids & catheters
  - washbowls
  - bedpans
  - endoscopes
  - ventilators & respiratory equipment
  - water, disinfectants etc

Sources of microbes/pathogens in NI

- **Reactivation of latent infection:** TB, herpes viruses
  - Less common
- **Endogenous:** normal commensals of the skin, respiratory tract, GI, GU tract
  - Common
- **Exogenous**
  - **Inanimate environment:** *Aspergillus* from hospital construction, *Legionella* from contaminated water
  - **Animate environment:** hospital staff, visitors, other patients
    - **Cross transmission- common**

Transmission

- **Contact**:
- direct (person-person),
- indirect (transmission through an intermediate object - contaminated instruments)

Cross transmission

- AIRBORNE: organisms that have a true airborne phase as pattern of dissemination (TB, Varicella)
- COMMON-VEHICLE: agent of transmission (ingested food or water, blood products, IV fluids)
- DROPLET: brief passage through the air when the source and patient are in close proximity
- ARTHROPOD

Hospital as microorganisms reservoir

- **Approximately 70% of NI involve drug-resistant bacteria**, which are common in hospital and nursing home as a result of the many antimicrobial agents that are used there.
- The drugs place selective pressure on the microbes, meaning that only those that are resistant to the drugs will survive.

The main microorganisms involved in NI – difficult to treat

- *Pseudomonas aeruginosa*
- Multi-drug-resistant *M. tuberculosis* (MDRTB)
- Vancomycine resistant *Enterococcus* species (VRE)
- Meticilline-resistant strains of *S. aureus* (MRSA) and *S. epidermidis.*

The main microorganisms involved in NI – difficult to treat

- Viruses: HIV
- Fungi: various *Candida* spp.
- Protozoa: malarial parasites

2001 - CDC

- Campaign to prevent antimicrobial resistance in health settings

CDC recommendations

- Prevent infection
- Diagnose and treat infection effectively
- Use antibiotics wisely
- Prevent transmission

CDC recommendations

- **Prevent infection**
- Diagnose and treat infection effectively
- Use antibiotics wisely
- Prevent transmission

Prevent infection

- **Step 1: vaccinate** (healthcare workers – influenza; *S. pneumoniae* vaccine to at-risk patients before discharge).
- **Step 2: get the catheter out** (use the catheter only when essential; use it correct; use proper insertion and catheter-care protocol; remove catheter promptly when they are no longer essential)

CDC recommendations

- Prevent infection
- **Diagnose and treat infection effectively**
- Use antibiotics wisely
- Prevent transmission

Diagnose and treat infection effectively

- **Step 3: target the pathogen** - target empiric therapy to likely pathogen; culture the patient; target definitive therapy to known pathogen: optimize timing, regimen, dose, etc.; monitor response and adjust treatment when is needed.
- **Step 3: access to expert** - consult infectious disease expert for patients with serious infections.

CDC recommendations

- Prevent infection
- Diagnose and treat infection effectively
- **Use antibiotics wisely**
- Prevent transmission

Use antibiotics wisely

- **Step 5: practice antimicrobial control** – engage in local antimicrobial appropriate-use programs.
- **Step 6: use local data** – know the S/R patterns (antibiograms) of local pathogens; know your hospital formulary; know your patient population.

Use antibiotics wisely

- **Step 7: treat infection, not contamination** – take care on sampling!
- **Step 8: treat infection, not colonization** – ex: treat pneumonia not tracheal aspirate; treat UTI not the indwelling catheter!
- **Step 9: know to say “no” to vancomycine** – MRSA may be sensitive to other antimicrobial agents; treat staphylococcal infection, not contamination or colonization!
- **Step 10: stop antimicrobial treatment** – when infection has been adequately treated; when infection is not diagnosed; when infection is unlikely.

CDC recommendations

- Prevent infection
- Diagnose and treat infection effectively
- Use antibiotics wisely
- **Prevent transmission**

Prevent transmission

- **Step 11: isolate the pathogen** – use standard infection control procedures; contain body fluids; follow airborne, droplet, and contact precautions; when in doubt, consult infection control expert.
- **Step 12: break the chain of contagion** – stay home when you are sick (healthcare worker); keep your hands clean!; set a good example!

Most Common Type of NI

- Urinary tract infections (UTIs)
- Surgical wound infections (also referred to as post-surgical wound infections)
- Lower respiratory tract infections (primarily pneumonia)
- Bloodstream infections (septicemia)

Different opinion regarding the second and third place?

Urinary tract infections (UTIs)

- Most common site of NI (40%).
- Affects 1/20 of admissions (5%)
- 80% related to urinary catheters.
- Incidence of nosocomial UTI is ~ 5% per catheterized day.
- Associated with 2/3 of cases of nosocomial Gram negative bacteremias

Urinary tract infections (UTIs)

- 25% of hospitalized patients will have a urinary catheter for part of their stay.
- Virtually *all patients develop bacteriuria* by 30 days of catheterization
- Of patients who develop bacteriuria, 3% will develop bacteremia
- Vast majority of catheter-associated UTIs are silent, but these comprise the largest pool of antibiotic-resistant pathogens in the hospital.

Safdar N. et al. *Current Infect Disease Reports* 2001;3: 487-495.

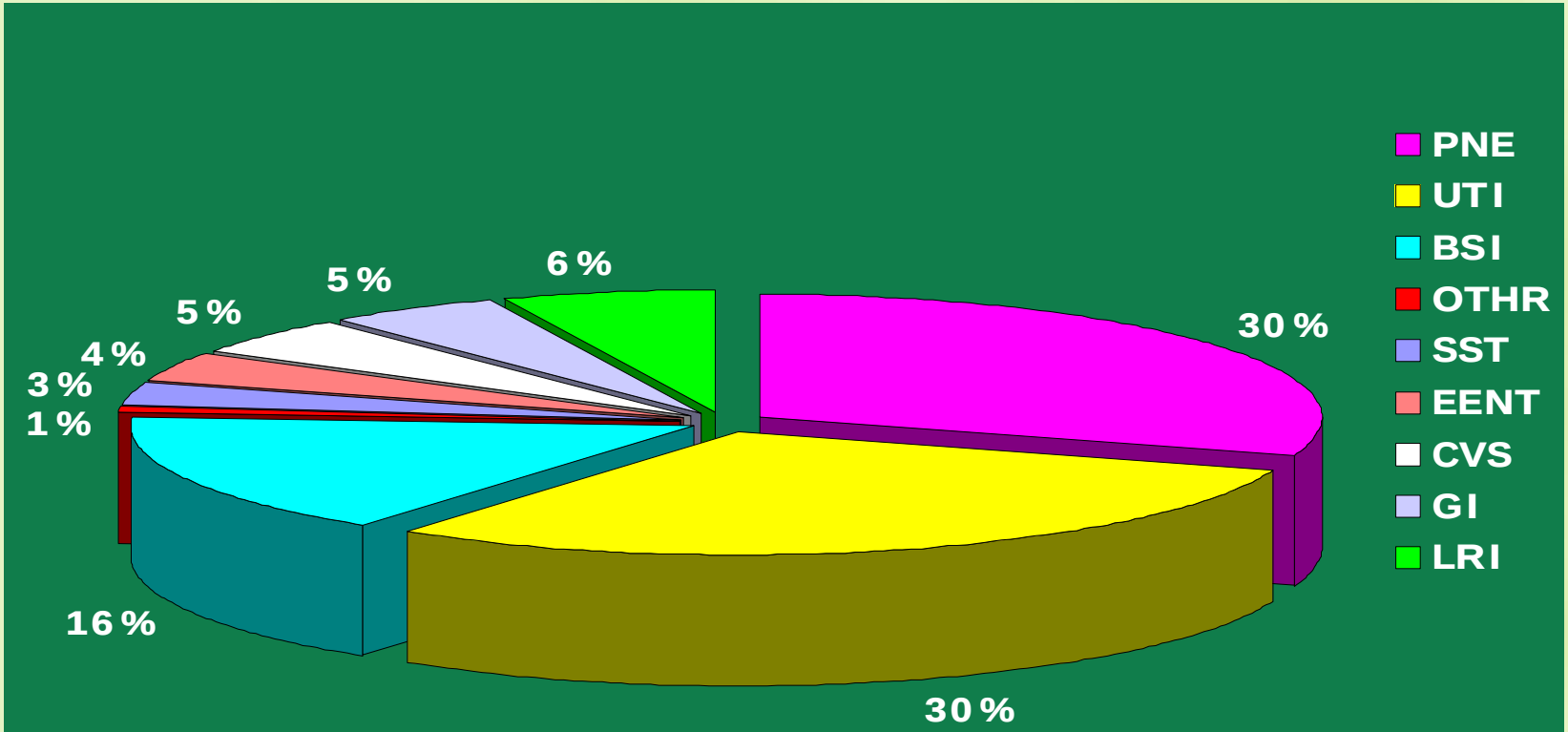
Urinary tract infections (UTIs)

- Source of uropathogens
  - **endogenous** - most common
    - catheter insertion
    - retrograde movement up the urethrea (70-80%)
    - patient's own enteric flora (*E. coli*)
  - **exogenous**
    - cross contamination of drainage systems
    - may cause clusters of UTI's

Urinary tract infections – catheter associated

E. coli	32%
Proteus spp	14%
Enterococcus	12%
Klebsiella	9%
Pseudomonas	9%
Enterobacter	4%
Candida	4%
Serratia	1%

Major sites of infection in medical ICU



n= 13,592 Nosocomial infections occur predominantly in Intensive Care Units

Richards MJ, et al. Infect Control Hosp Epidemiol 2000; 21: 510-515

Patients Most Likely to Develop NI

- Elderly patients
- Women in labor and delivery
- Premature infants and newborns
- Surgical and burn patients
- Diabetic and cancer patients
- Patients receiving treatment with steroids, anticancer drugs, antylim-phocyte serum, and radiation.

Major Factors Contributing to NI

- An ever-increasing number of drug-resistant pathogens.
- The failure of healthcare personnel to follow infection control guidelines.
- An increased number of immunocom-promised patients.

Additional Contributing Factors:

- The indiscriminate use of antimicrobial agents, which has resulted in an increase the number of drug-resistant and multi-drug-resistant pathogens.
- A false sense of security about antimicrobial agents, leading to a neglect of aseptic techniques and other infection control procedures.
- Lengthy, more complicated types of surgery.
- Overcrowding of hospitals and other healthcare facilities as well as shortages of staff.

Additional Contributing Factors:

- Increased use of less-highly trained healthcare workers, who are often unaware of infection control procedures.
- Increased use of anti-inflammatory and immunosuppressant agents, such as radiation, steroids, anticancer chemotherapy, and antilymphocyte serum.
- Overuse and improper use of indwelling medical devices.

What Can Be Done To Reduce the Number of NI?

- Handwashing is the single most important measure to reduce the risks of transmitting from one patient to another or from one anatomical site to other on the same patient.

Handwashing

- Wash your hands **before** you:
- prepare or eat food;
- treat a cut or wound or tend to someone who is sick;
- insert or remove contact lenses.

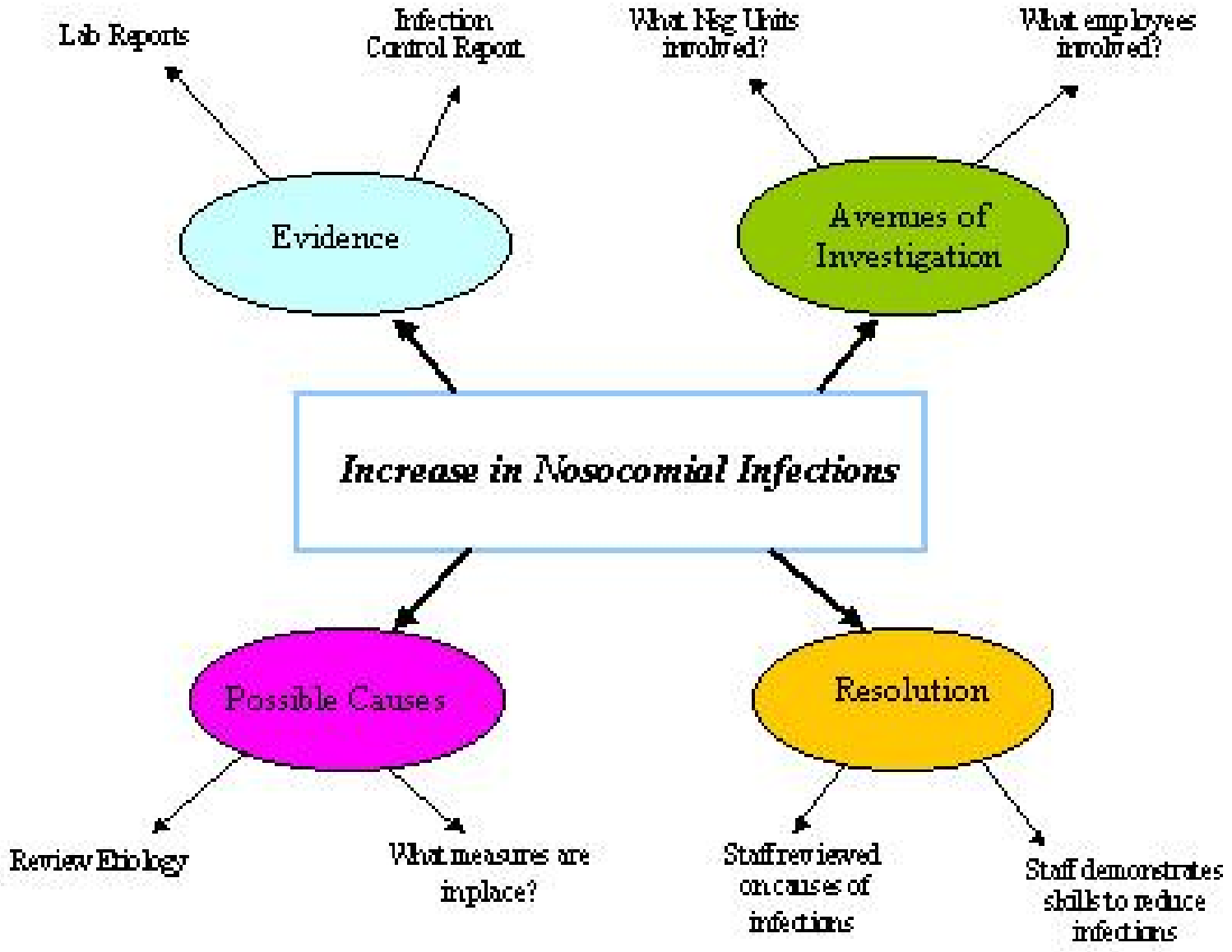
Handwashing

- Wash your hands **after** you:
- use the restroom;
- handle uncooked foods, particularly raw meat, poultry, or fish;
- change a diaper;
- cough, sneeze, or blow your nose;
- touch a pet, particularly reptiles and exotic animals;
- handle garbage;
- tend to someone who is sick or injured.

Handwashing

- Wash your hands **in the following manner**:
- use warm or hot, running water!
- use soap (preferably an antibacterial soap)!
- wash all surfaces thoroughly, including wrists, palms, back of hands, fingers, and under fingernails (preferably with a nail brush)!
- rub hands together for at least 10 to 15 seconds!
- when drying, begin with your forearms and work toward your hands and fingertips, and pat your skin rather than rubbing to avoid chapping and cracking!

PROBLEM MAP FOR NOSOCOMIAL INFECTION



Role of the Microbiology Laboratory in Hospital Epidemiology and Infections Control

- Clinical Microbiology Laboratory (CML) personnel participate in infection control in three major ways:
- by monitoring the types and numbers of pathogens isolated from hospitalized patients
- by notifying the appropriate Infection Control Professional (ICP) should an unusual pathogen or an unusually high number of isolates of a common pathogen be detected. The ICP will initiate an investigation of the outbreak.

Role of the Microbiology Laboratory in Hospital Epidemiology and Infections Control

- By processing environmental samples, including samples from hospital employees (e.g. nasal swabs), that have been collected from within the affected ward(s).
- It is hoped that this will pinpoint the exact source of the pathogen that is causing the outbreak.

Role of the Microbiology Laboratory

- Two most commonly methods have been used: biotype and antibiogram.
- If two or more strains produce the exact same biochemical test results, they are said to have the same **biotype**.
- If they produce the exact same susceptibility and resistance patterns when antimicrobial susceptibility testing is performed, they are said to have the same **antibiogram**.

Role of the Microbiology Laboratory

- Having the same biotype and antibiogram is evidence, but not absolute proof, that they are the same strain.
- Due to the limitations of PHENOTYPIC METHODS, most hospital/laboratories used MOLECULAR EPIDEMIOLOGY, in which GENOTYPIC METHODS are used.

Role of the Microbiology Laboratory

- Molecular techniques for establishing the presence or absence of clonality can be very effective in tracking the spread of infections caused by genetically related pathogens.

References (molecular methods)

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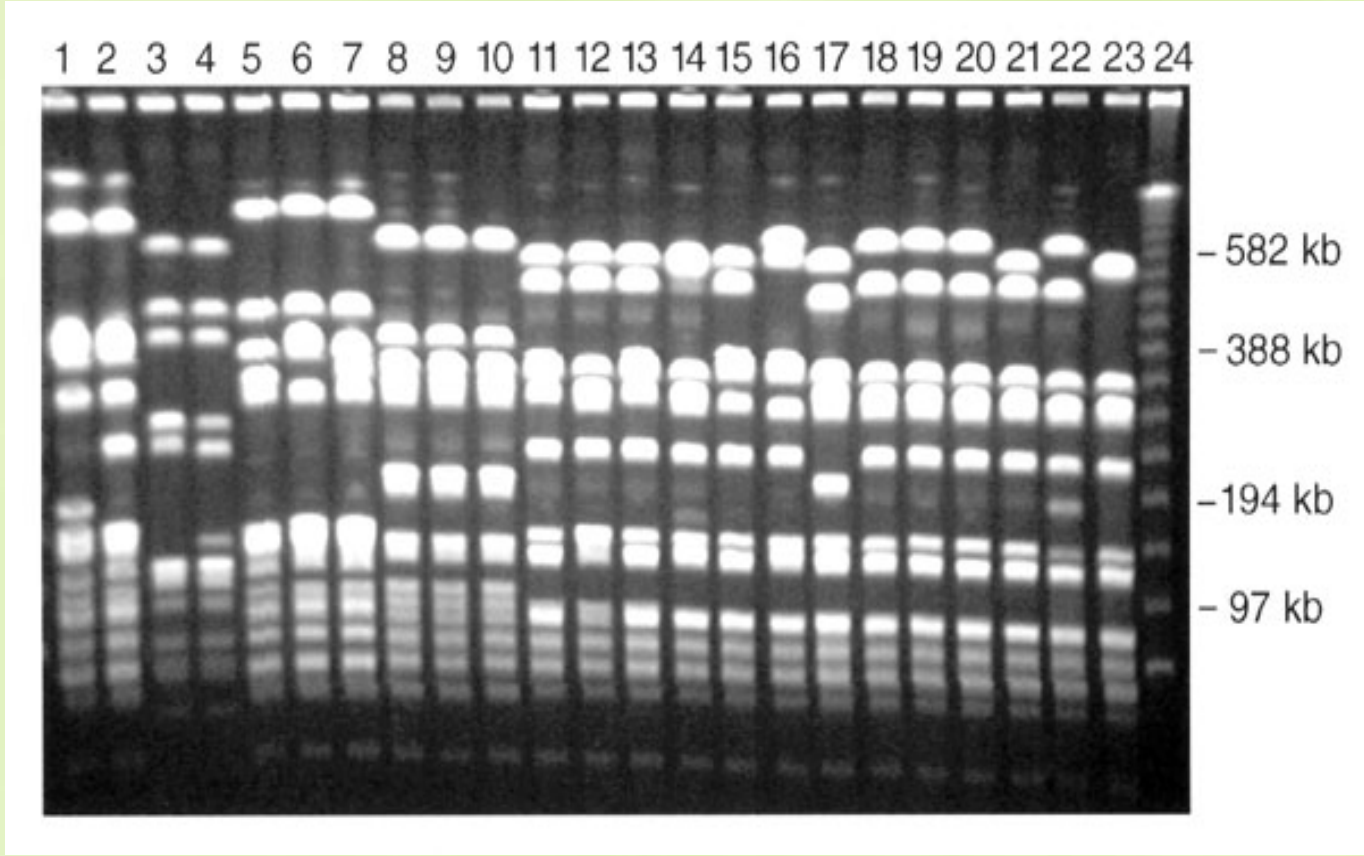
Pulsed-field gel electrophoresis (PFGE)



- **Figure.** Pulsed-field gel electrophoresis (PFGE) profiles of *Staphylococcus aureus* isolates digested with Sma 1. A variety of PFGE profiles are demonstrated in these 23 isolates.

Infection Control Committees and Infection Control Professionals

- All healthcare facilities should have some type of formal infection control program in place.
- Its functions will vary from one type of healthcare facility to another.
- In a hospital setting, the infection control program is usually under the jurisdiction of hospital's Infection Control Committee (ICC) or Epidemiology Service.

ICC

- Representatives from most of the hospital's departments including: medical and surgical services, pathology/microbiology, nursing, hospital administration, pharmacy, housekeeping, food services, etc.
- Chairperson - an Infections Control Professional (ICP): physician (ex. an epidemiologist, infectious disease specialist, microbiologist), an infection control nurse, etc.

ICC's responsabilities

- Periodically reviews the hospital's infection control program and incidence of NI.
- It is a policy-making and review body that may take drastic action (ex. Instituting quarantine measures) when necessary.
- Patients and environment surveillance.
- Investigation of outbreaks/epidemics.
- Education of hospital staff regarding infection control.

Conclusions

- Nosocomial infections are a major challenge for healthcare facilities.
- The risk of epidemic evolution impose:

- rapid diagnosis using molecular techniques for clonality analysis;
- accurate epidemiological surveillance;
- preventive methods according with NI guidelines.

Thank you!