

Do we need clinical ID guidelines targeted to aged persons?

ESCMID Postgraduate Education Course
Infection Management in the Elderly:
Room for Improvement
Annecy, France
2 – 3 October 2014

Where do differences exist?

Vaccines

- Incidence of vaccine-preventable diseases higher
 - Influenza, VZV, *Streptococcus pneumoniae*
- Vaccine immunogenicity lower
- Infection-related morbidity and mortality of vaccine-preventable diseases higher

Infection control/ antibiotic stewardship

- Higher exposure to healthcare settings
- Higher exposure to catheters and other foreign devices
- Higher likelihood of clinical infections caused by acquired MDR bacteria
- More frequent need for antibiotics and antibiotic use
 - Higher likelihood of MDR colonization persistence

Infection diagnosis

- Baseline probabilities of the different sources of infections
- Time from onset of infection to presentation
- Sepsis symptoms
- Sepsis signs
- Biomarkers

Sepsis presentation in the elderly

- Prospectively cohort study
- Overall, 4308 patients with suspected community-onset and hospital-acquired bacterial infections
- Data collected between 2002-2004 and 2010-2011 as part of the development and testing of TREAT – a decision support system for antibiotic treatment, at Beilinson Hospital
- We compared the presentation of elderly patients (≥ 75 years) versus adults (< 75 years).

Yahav et al. submitted for publication

Author	Journal, year	Population	Results
Terpenning et al.	Am J Med 1987	53 >60 yrs. vs. 55 <60 with endocarditis	↓ Symptoms
			↓ Febrile response
			↑ Error in diagnosis (68%)
Werner et al.	Am J Med 1996	28 <50 yrs. vs. 58: 50-70 vs. 20>70 yrs. with endocarditis	↓ Fever ↓ Leukocytes
Marrie et al.	J Am Geriatr Soc 1985	81>65 yrs vs. 57<65 yrs. hospitalized with CAP	↓ Febrile response (57% vs. 26%)
Tiruvoipati et al.	BMC geriatrics 2010	567<65 yrs vs. 108>65 yrs with sepsis in ICU	↓ Fever
			- Leukocytes
			↑ SBP
			↑ APACHE, creatinine
Cooper et al.	Clin Infect Dis 1994	Intra-abdominal infections	↓ Fever, leukocytes
			↓ Leukocytes
			↓ GI symptoms
			↑ Duration of symptoms

Author	Journal, year	Population	Results
Finklestein et al.	J Am Geriatr Soc 1983	> 65 yrs. vs. younger (total 187) with pneumococcal bacteremia	↓ Fever
			- Leukocytes
			- Heart rate
Chassagne et al.	Am J Med 1996	71>65 yrs. vs. 34 <65 yrs. with bacteremia	↓ Fever
			↓ Chills
			↑ Altered mental status
			- Heart rate
Paul et al.	Unpublished	463>80 yrs. vs. 652: 65-80 yrs. vs. 550<65 yrs. with <i>S. aureus</i> bacteremia	↓ Fever
			↑ Leukocytes
			↑ Septic shock
Lee et al.	Medicine 2007	415<65 yrs. vs. 406: 65-85 yrs vs. 69>85 yrs with community-onset bacteremia	↓ Fever
			↑ Dyspnea
			↑ Acute renal failure
			↑ Leukocytes

Summary of sepsis presentation studies

- Mostly retrospective studies, conducted many years ago, mostly small

Sepsis presentation in the elderly	n/N studies
Less fever	6/10
Altered mental status	3/3
Shock	2/3
Respiratory distress	1/2
Less leukocytosis	4/8
Renal failure	4/5

Possible bias in estimation of 'atypical' sepsis presentation in the elderly

- Observational studies portray real life and in real life physicians work under the assumption that sepsis presents atypically in the elderly and thus bias results towards fewer sepsis signs in the elderly
 - Referral to the hospital
 - Blood culture sampling
 - Diagnosing infections
- Presentation different because pathogens and diagnoses are different
- Oral/ axillary temperature measurements unreliable in the elderly

Antibiotic treatment

No difference

- Type of antibiotic determined by bacteria and site of infection
- Dosing is dependent on many factors. But is it dependent on age per se?

Possible difference

- Time to treatment
- Duration of treatment
- Toxicity
- Site of care and duration of hospital stay
- Follow-up and rehabilitation post-infection

Non-antibiotic sepsis management

- Hydration strategy
- Effects and toxicity of catecholamines
- Corticosteroids
- Immunoglobulins
- Glucose control
- Nutrition
- DVT prophylaxis

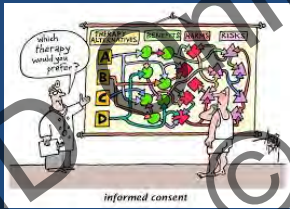
Surviving Sepsis Campaign

International Guidelines for Management of Severe Sepsis and Septic Shock: 2012 Table of Contents

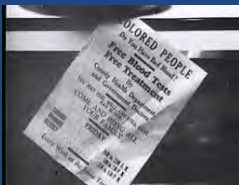
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Research

- Informed consent
- *Methods of follow-up*
- *Outcomes measured*



Research - 1932



The New York Times

Syphilis Victims in U.S. Study Went Untreated for 40 Years

By JEAN HEILBR

WASHINGTON, July 25—For 40 years the United States Public Health Service has conducted a study in which human beings have been infected with syphilis, who were induced to serve as guinea pigs, have gone without medical treatment for the disease, and a few have died of its late effects, even though an effective therapy was eventually discovered.

The study was conducted to determine from autopsies what the disease does to the human body.

Officials of the health service who initiated the experiment have long since retired. Current officials, who say they

have serious doubts about the morality of the study, also say that it is too late to treat the victims in any surviving participants.

Doctors at the service say they are now studying what other medical services they can give to the survivors with the hope of the disease's effects curbing.

In Mobile, Ala., Assistant Secretary of Health, Education and Welfare for Health and Scientific Affairs, expressed shock on learning of the study. He said that he was making an immediate investigation.

The experiment, called the Tuskegee Study, began in 1932 with about 600 black men

Research – 2014

DRAFT GUIDELINES ON AUDIO-VISUAL RECORDING OF INFORMED CONSENT PROCESS IN CLINICAL TRIAL

CENTRAL DRUGS STANDARD CONTROL ORGANIZATION
DIRECTORATE GENERAL OF HEALTH SERVICES
MINISTRY OF HEALTH & FAMILY WELFARE
GOVT. OF INDIA
9th JAN, 2014



Participation of elderly patients in RCTs addressing antibiotic treatment of pneumonia

- Systematic review of RCTs published between 2005-2013
- We examined whether:
 - Age or other attributes that might preferentially exclude the elderly, form part of RCTs' inclusion and exclusion criteria
 - Separate analyses of the elderly were performed in RCTs for the relevant outcomes
 - Results in RCTs for the elderly and younger adults were different
 - The elderly were actually represented in RCTs as they are in clinical practice.

Avni et al. Submitted for publication

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author

Treatment effects

- Trials that reported on clinical failure (primary outcome) for age groups
- Calculated the risk ratio with 95% CI for pooled effects of intervention vs. control in the elderly and younger adults, using methods of indirect meta-analysis
- All trials: between groups risk ratio **1.25 (95% CI 0.94-1.65)**. Cutoff 65 years.
- Subgroup same trials: between groups risk ratio **1.43 (95% CI 0.98-2.09)**. Cutoff 75 years.
- No subgroup reporting for mortality, length of stay or other outcomes

Where are guidelines needed?

Address a real need
Evidence exists to back guidelines

Research conduct

Testing new/ high risk intervention

Patient informed consent

Testing of standard of practice

Transfer decision to national/ other ethics review committee

Re-examine relevant outcomes

Antibiotic treatment of moderate-severe community-acquired pneumonia: design and rationale of a multicentre cluster-randomised cross-over trial.

- In an ideal comparison of empirical antibiotic therapies, the allocation of treatment would be unrelated to patient and disease characteristics, to ensure comparability of the treatment groups in terms of prognosis.
- Additionally, the timing of treatment and of concomitant therapy should be comparable with clinical practice.
- When studying empirical antibiotic treatment of CAP, the first requirement is not satisfied in observational studies, while RCTs do not comply with the second.

van Werkhoven CH1, Postma DF, Oosterheert JJ, Bonten MJ. Neth J Med. 2014 Apr

- To overcome these limitations, we have designed a multi-centre cluster randomised cross-over study, comparing empirical antibiotic strategies.
- Participating centres are randomised to three consecutive periods of four months, in which one of the three empirical antibiotic strategies applies.
- In each hospital the local antibiotics committee has been asked to adopt this empirical strategy as the standard treatment for CAP during that period.
- The medical ethics review board judged that this cluster-randomised study is not liable to the same regulations as an individually randomised trial.
- Consequently, written informed consent is not needed prior to the start of the preferred treatment of the study, but only for collection of individual patient data.
- Importantly, this is only legitimate for interventions that are registered for the disease under study and are considered equally effective.

Infection control/ antibiotic stewardship

- Infection control in rehabilitation centers
 - Contact isolation in the context of rehabilitation
 - Post-discharge care
- Antibiotic stewardship in the elderly
 - Reduce unnecessary antibiotic use
 - Target appropriate empirical antibiotic treatment for severe infections
 - Try for shorter, outpatient treatment

Antibiotic treatment

- Need for antibiotics
- Importance of empirical antibiotic treatment
- Antibiotic dosing
- Duration of antibiotic treatment, intravenous vs. oral treatment
- Site of care
- Rehabilitation post-infection



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Surviving sepsis

- Hydration strategy
- Catecholamines
- Corticosteroids
- Immunoglobulins
- Glucose control
- Nutrition
- DVT prophylaxis

Thank you

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