

# CA-MRSA Definition (CA, HA, LA) and epidemiology

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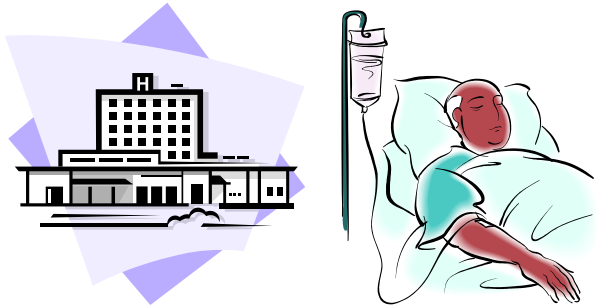
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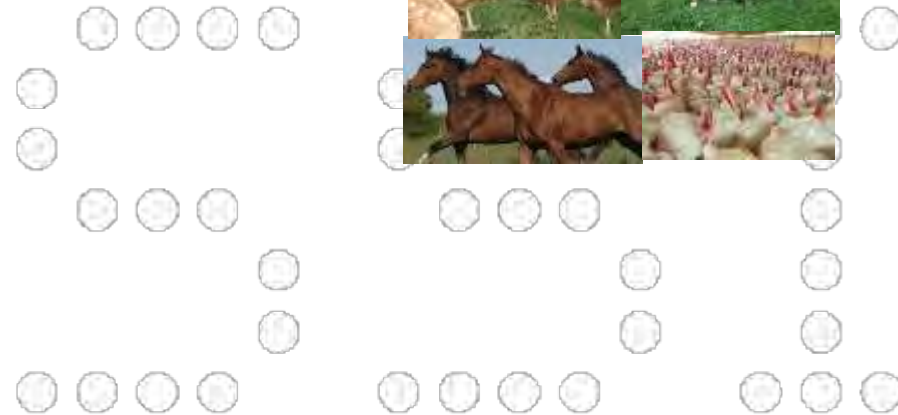
# EPIDEMIOLOGY OF MRSA

## HA - MRSA

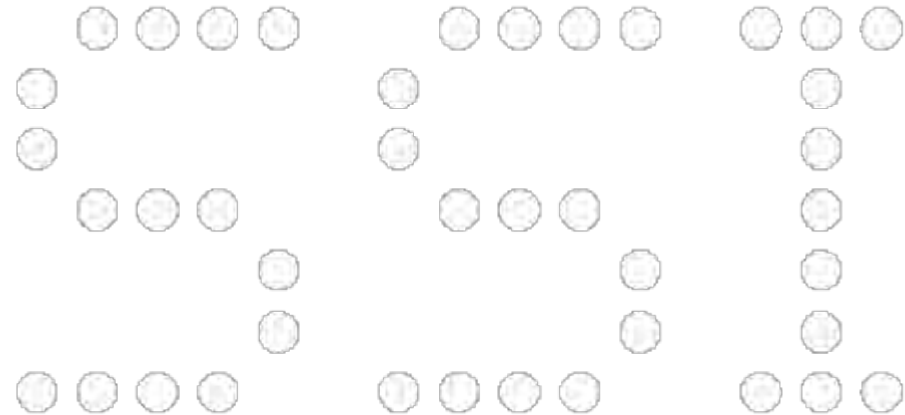
## LA - MRSA



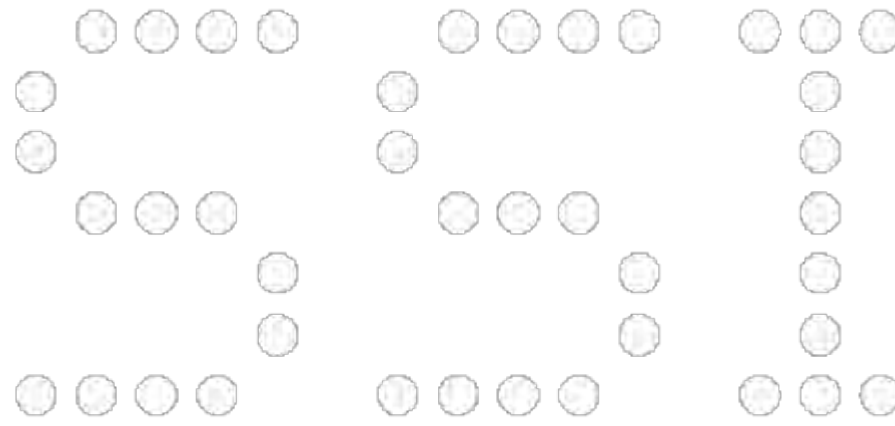
## CA - MRSA



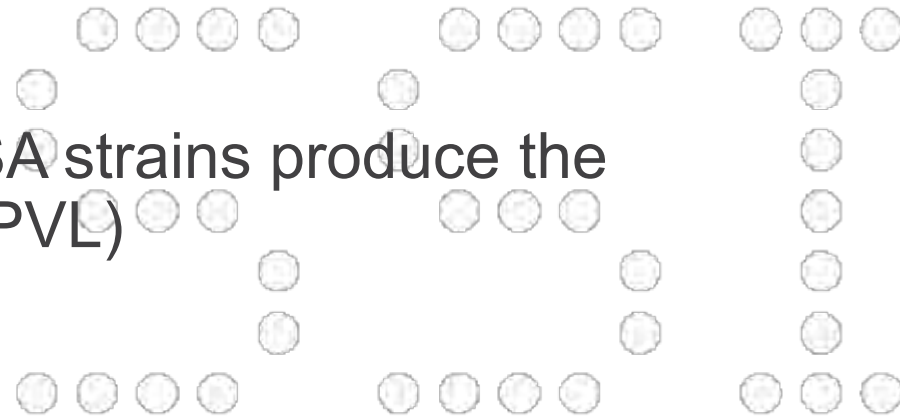
- In the late 1990s the epidemiology of MRSA infections began to change
  - **from** being almost exclusively a health care associated infection
  - **to** also cause infection in otherwise healthy persons without any connection to health care



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- ❖ Large diversity of strains, distinct lineages – not just feral descendants of HA-MRSA strains,
  - at present <10 lineages are found worldwide including
    - ST1-IV (USA400); ST8-IV (USA300); ST30-IV (Pacific/Oceania); ST59-IV and V (USA1000, Taiwan); ST80-IV (European) and CC398 from production animals
- ❖ SCC *mec* type IV
  - type V, new variants
- ❖ Often less multiresistant
  - At least used to be
- ❖ Most of the dominant CA-MRSA strains produce the Panton–Valentine leukocidin (PVL)



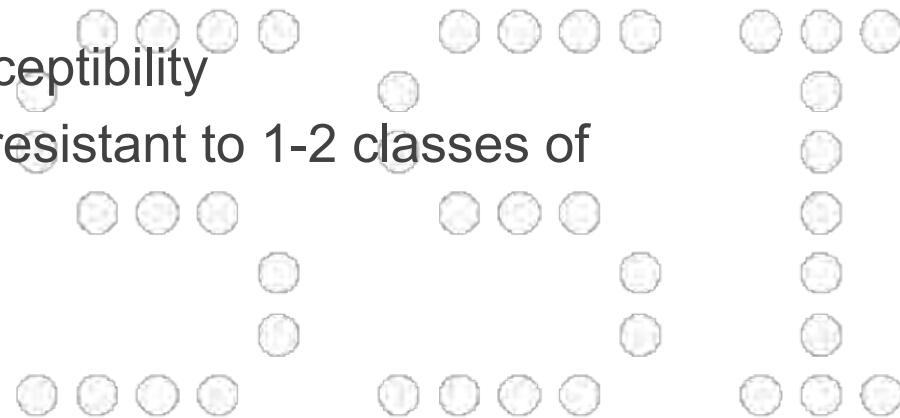
❖ However no single definition exists for CA-MRSA and none of the definitions are perfect!

- Epidemiological

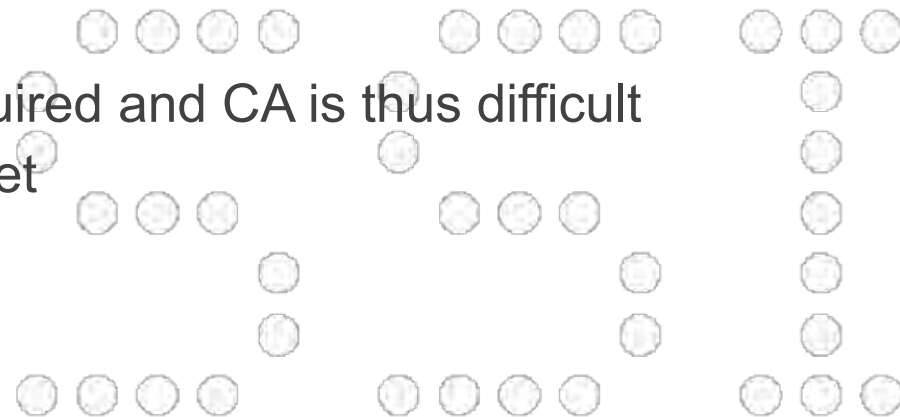
- Community onset and lack of health care-associated risk factors (CDC 2000)
  - Exclusion if previous MRSA positive.....

- Microbiological

- SCC*mec* IV (V)
- Clindamycin/ciprofloxacin susceptibility
- Non-multidrug resistant (only resistant to 1-2 classes of antibiotics)
- PVL positive

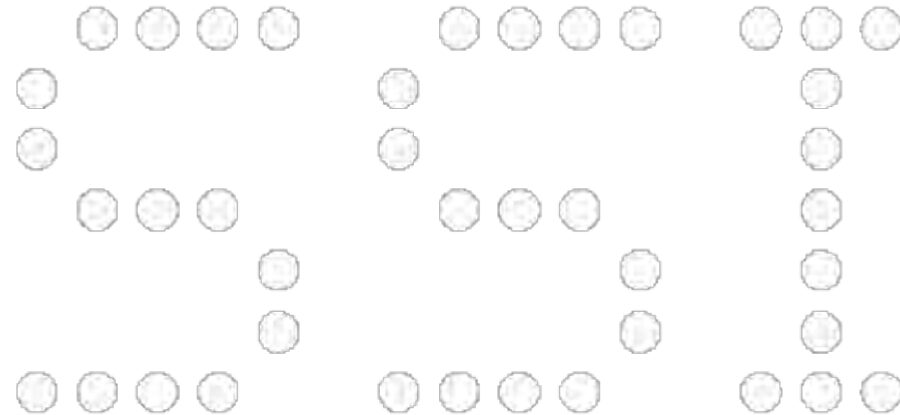


- ❖ The definition is further complicated by
  - *S. aureus*/MRSA can be carried for prolonged time without/before causing infections
    - 80% of bacteraemias are endogenous i.e. caused by the same strain as the person carries
- ❖ Acquisition
  - Time and place where
    - the infection starts?
    - the MRSA strain is acquired?
- ❖ Differentiation between hospital-acquired and CA is thus difficult
  - Hospital onset vs community onset



# DEFINITION OF CA-MRSA

- Definition of CA-MRSA is therefore to a large extent based on a combination of microbiological characteristics and absence of risk factors for being
  - hospital acquired
  - livestock-associated

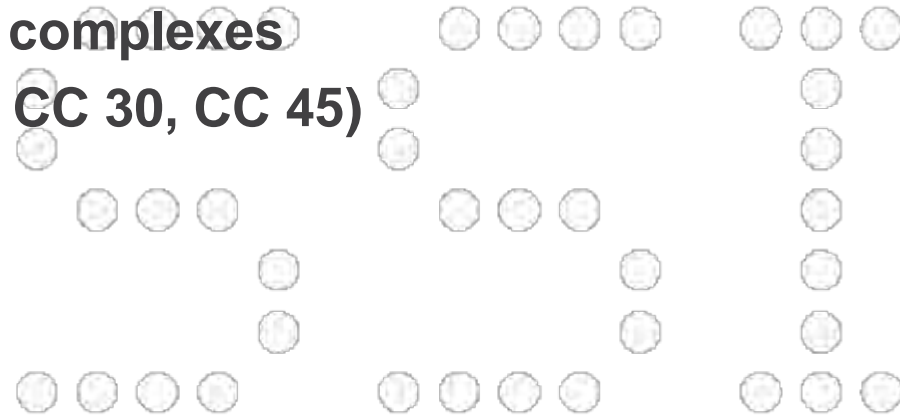




## ❖ HA-MRSA

- 1. MRSA wave (1961- early 1970ies)
  - *Sccmec* I – Some European countries + Australia
- 2a. MRSA wave (late 1970ies -)
  - *Sccmec* II and III / CC5, CC8, CC30 (ST36)
- and 2b. MRSA "wave" (late 1980ies -)
  - *SCCmec* IV in novel / known HA- clones
    - CC22, CC45 / CC5 and CC8

**>90% of MRSA world wide belongs  
to only 5 clonal complexes  
(CC 5, CC8, CC 22, CC 30, CC 45)**

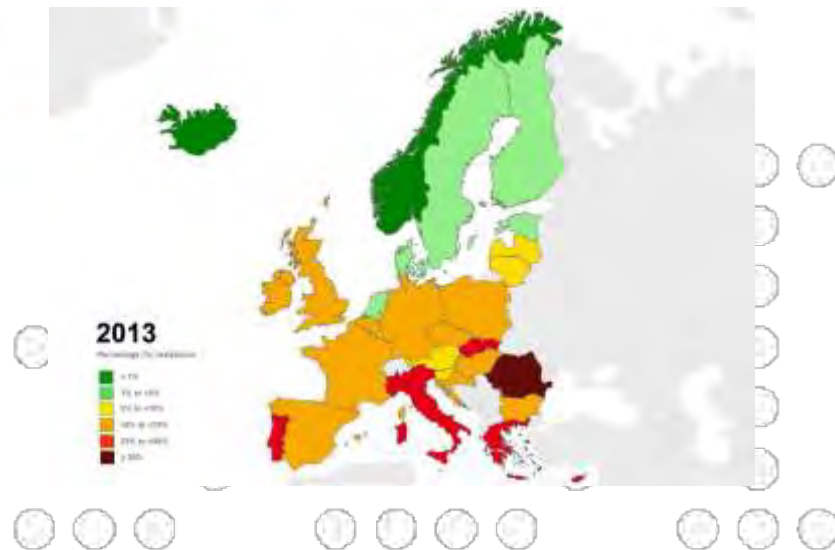
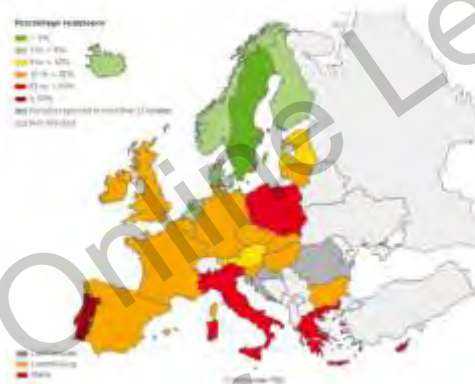


# MRSA BACTEREMIA EUROPE

Proportion of Methicillin Resistant *Staphylococcus aureus* (MRSA) Isolates in Participating Countries in 2007



Proportion of Methicillin Resistant *Staphylococcus aureus* (MRSA) Isolates in Participating Countries in 2012



## ❖ 3.rd wave

- CA-MRSA (late 1980ies – (early1980ies -))
  - Acquisition of the *SCCmec* IV and other small *SCCmec* cassettes into new strains including different lineages
    - Australia – aboriginal communities
    - Solitary reports of CA-MRSA in Europe
      - » Two reports from US in the early 1980s (US)

## ❖ In August 1999 MMWR reported the death of 4 children due to CA-MRSA

- Changed the perception of CA-MRSA from being an oddity to be a real and significant phenomenon!



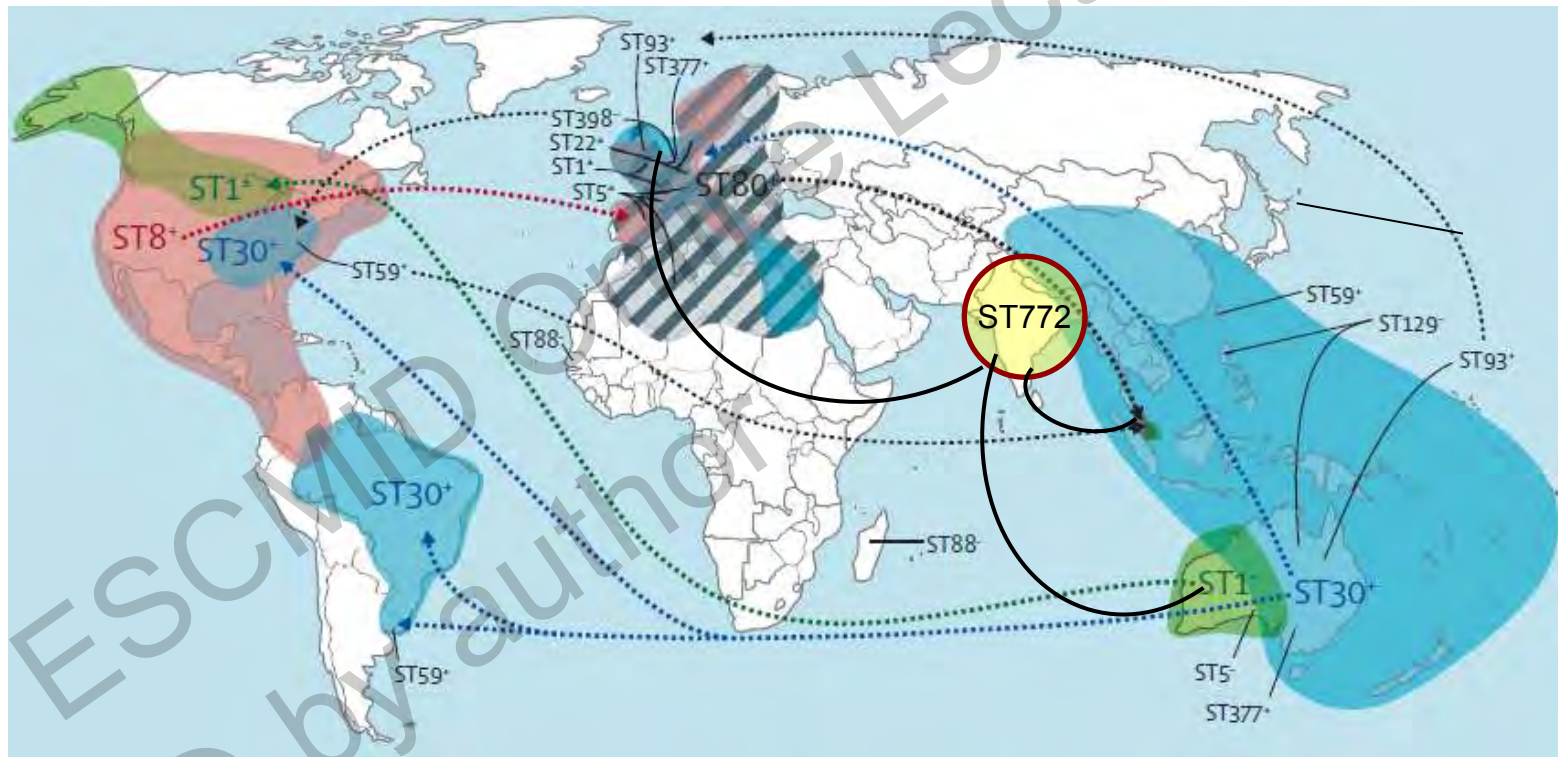
## ❖ Worldwide significant problem beginning in the late 1990s

## ❖ The appearance of CA-MRSA represents a paradigm shift in MRSA epidemiology!

# DOMINATING CA-MRSA SEQUENCE TYPES

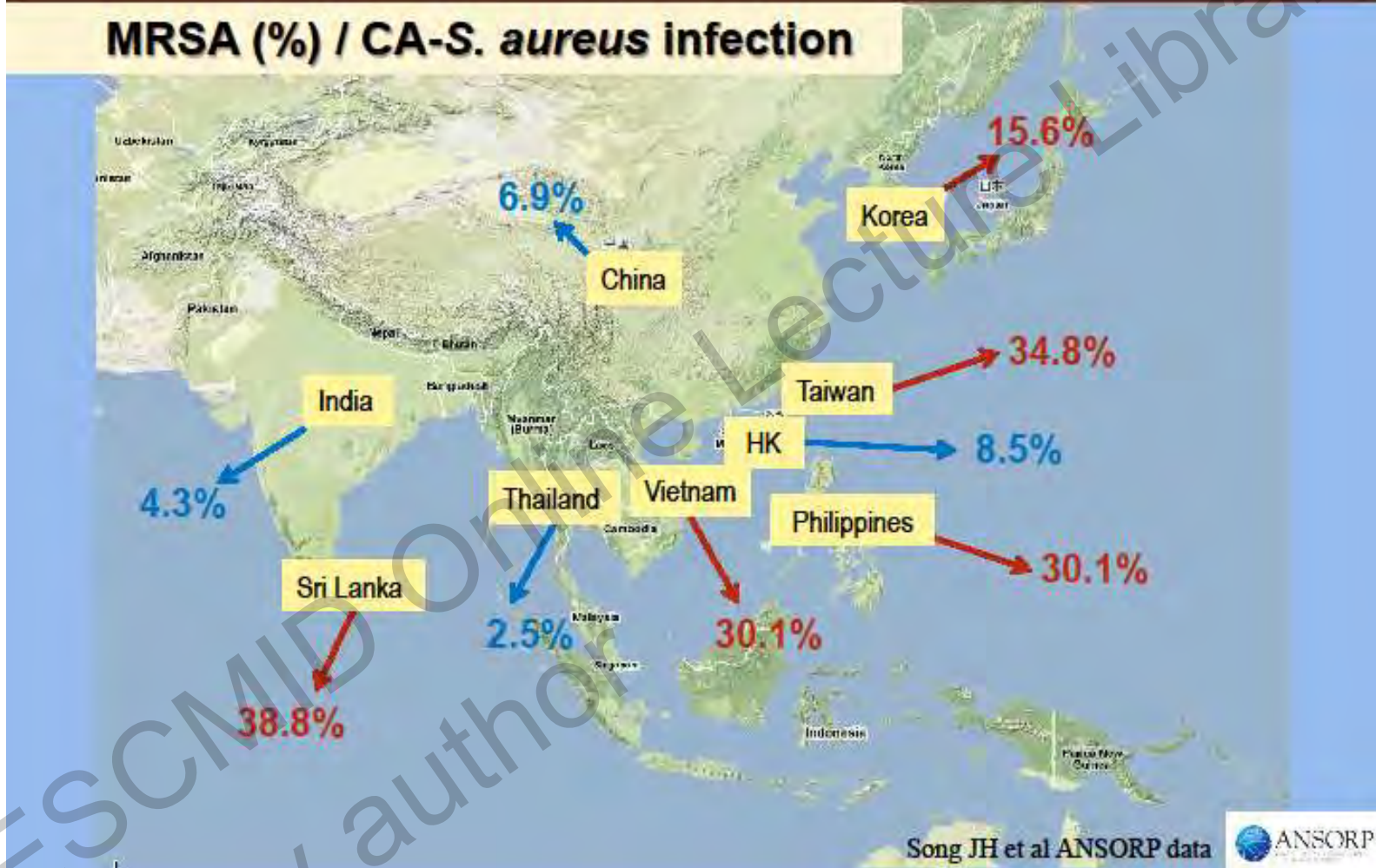
## ❖ 5 lineages spreading worldwide

- ST1-IV (USA400); ST8-IV (USA300); ST30-IV (Pacific/ Oceania); ST59-IV and V (USA1000, Taiwan); ST80-IV (European),
  - recently spread of ST772 (Bengal Bay clone)



# MRSA in Asian countries

## MRSA (%) / CA-S. aureus infection



## Traditional risk factors for nosocomial MRSA infection

- ❖ Previous hospital stay
- ❖ Prolonged length of stay prior to infection
- ❖ Surgical procedure(s)
- ❖ Enteral feeding
- ❖ Previous antibiotic use
- ❖ Central venous catheter insertion
- ❖ History of MRSA

## Risk factors for community-associated (CA) MRSA

- ❖ History of colonization/infection with CA-MRSA
- ❖ Close contact with a person colonized/infected with CA-MRSA
- ❖ Indigenous people
- ❖ Especially from US literature
  - Adults  $\geq 65$  years; children  $< 2$  years
  - “special communities”
  - Participation in contact sports
  - Injection drug use
  - Living in correctional facilities or shelters
  - Military personnel
  - Men who have sex with men

# COMMON RISK FACTORS IN POPULATIONS AT HIGHEST RISK

❖ One or more of the following are characteristic of the populations at highest risk

- frequent Antibiotic use and overuse
- Poor hygiene / **C**leanliness
- **C**ompromised skin
- Frequent skin **c**ontact
- **C**ontaminated surfaces and shared items
- **C**rowding (up to 7.5 persons per bedroom)

❖ **These groups amplify MRSA!**

- MRSA is likely to disseminate from these communities to the population in general



# CHARACTERISTICS OF CA-MRSA INFECTIONS

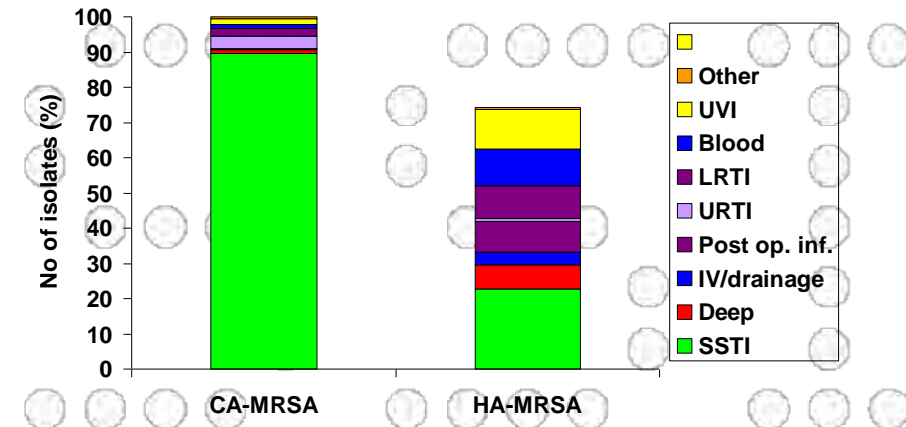
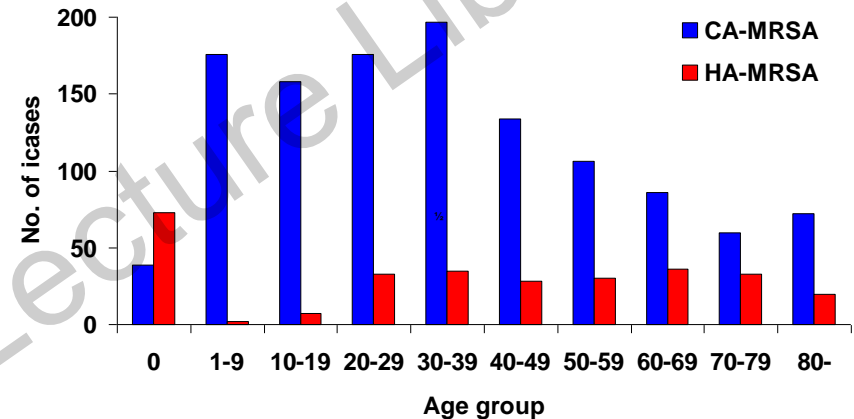
❖ Often seen in children, adolescents and younger adults

- (parents and grandparents)

❖ Dominated by SSTI

- Expected as these mostly affects otherwise healthy persons

❖ Severe infections including necrotizing pneumonia, fasciitis and bacteremia are also seen!





## ❖ Europe

- Belgium 3%, Denmark, Germany, The Netherlands and Portugal, approximately 0.1% - 0.3%

## ❖ Australia

- 0.7%

## ❖ US

- MRSA carriage increased from 0.8% in 2000-1 to 1.55% in 2003-4 (NHANES)
- Mexico 8.6%, Hawaii, 3%

## ❖ Asia

- Taiwan 9.0% Japan 3.5%

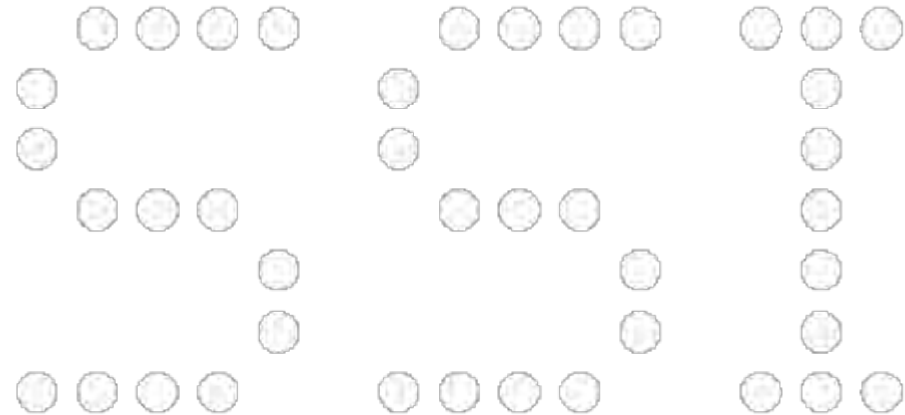
# EVIDENCE OF CA-MRSA AS CAUSE OF HAI

- ❖ Greece, ST80 caused 25% of hospital-acquired infections in 2004
- ❖ USA the epidemiology both in the community but also increasingly in hospitals is dominated by ST8-IV, spa type t008 (USA300)
- ❖ Taiwan, ST59 V<sub>T</sub> caused 13% of HA-MRSA and 47% of HACO infections

Chini V *et al. Scand J Infect Dis* 2008;40:368–372  
Seybold, *CID*, 2006; 42:647–56 Klevens, *CID*, 2006;  
42:389–91; Miller, *Emerg Inf Dis* 2007;13,236-42;  
Huang, *CMI*,2008;14:1167-72

- ❖ 4.th MRSA “wave” (2004 - )
  - LA-MRSA
    - CC398
    - ( $mecA_{LGA251}$ )

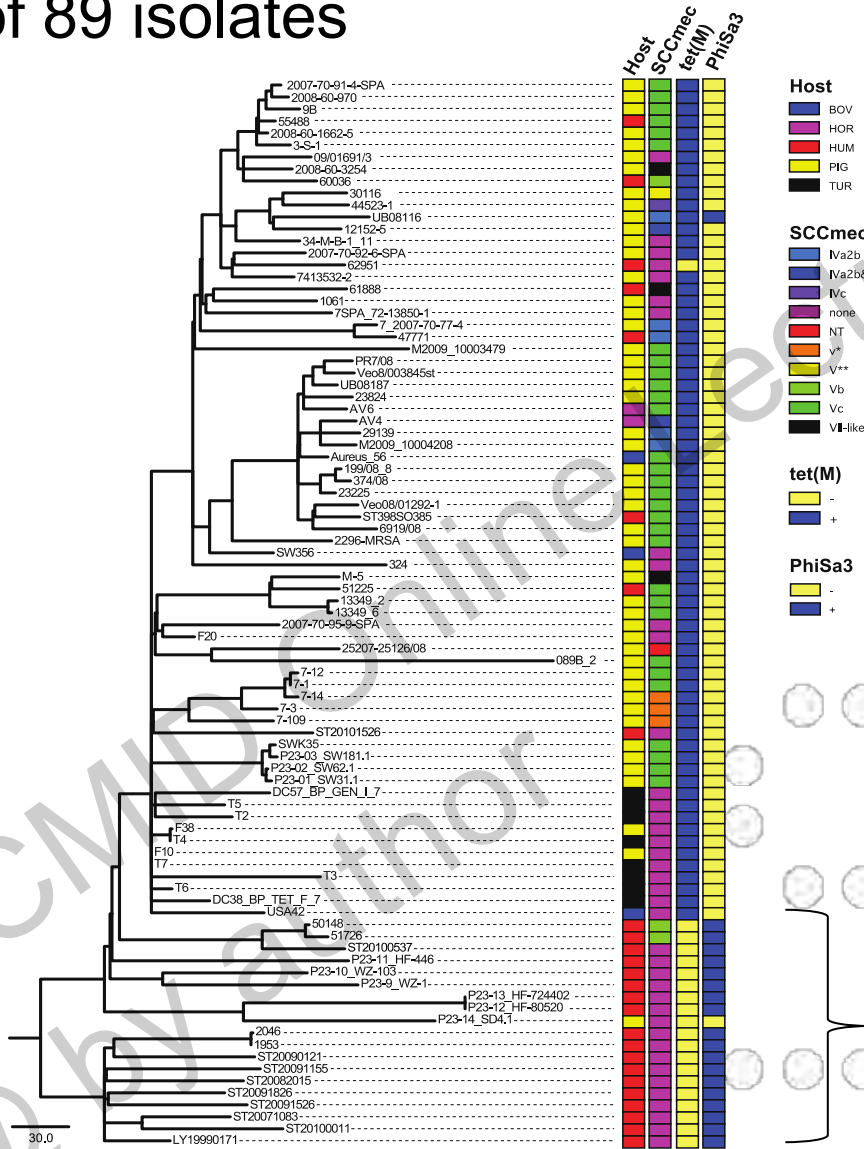
**yet another paradigm shift!**



- ❖ MRSA in animals has been known since 1972
  - MRSA in a cow
- ❖ Livestock associated MRSA was recognized as a true zoonotic reservoir in 2004/5
  - CC398 in Holland and France
- ❖ CC398 –is today reported from most parts of the world – and is by far the most prevalent type of LA-MRSA
  - Pigs is the main reservoir
  - In Belgium, Holland and Germany veal calves is also a large reservoir
  - Also found in chickens, turkeys, dairy cows and horses
    - » Dogs, rats

# FROM HUMAN MSSA TO LA-MRSA

## WGS of 89 isolates



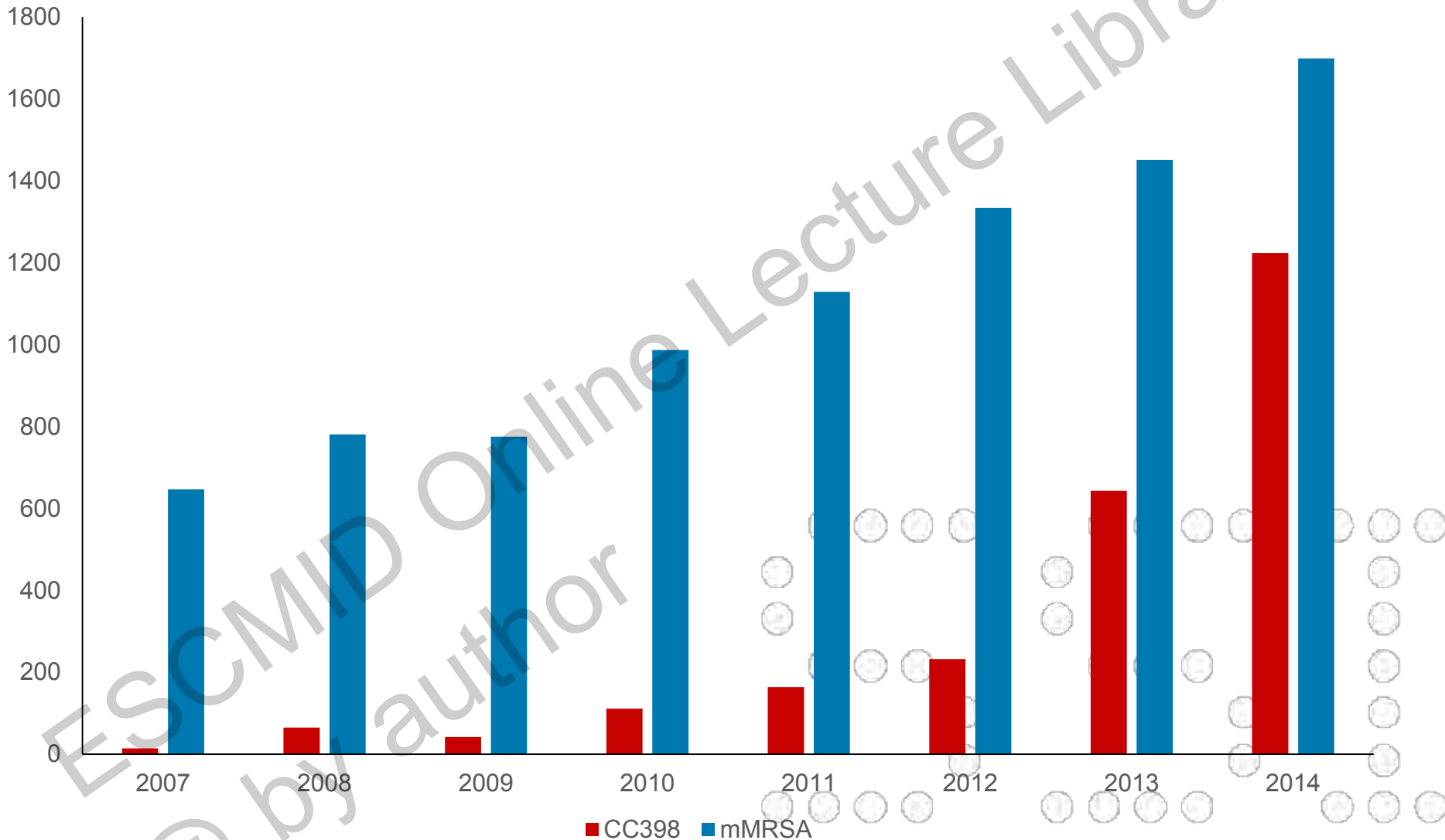
- Host**
- BOV
  - HOR
  - HUM
  - PIG
  - TUR
- SCCmec**
- Iva2b
  - Iva2b&5
  - Ivc
  - none
  - NT
  - v+
  - v++
  - Vb
  - Vc
  - VI-like
- tet(M)**
- - +
- PhiSa3**
- - +

Basal clade

- Human
- MSSA
- tet S
- phiSa3

Price, mbio, 2012

# MRSA CASES HUMAN VS LA-MRSA, DENMARK



## ❖ Multifactorial!

### - Trade

- 79% vs 23% for supplying herd being positive resp. negative OR 10.8 (1.5-110.1) –
  - But 23% with negative supplier and 46% without supplier was positive

### - Herd size

### - Antimicrobials

- Selection pressure results in numerous of different resistance patterns, several different *SCCmec* types – some only found in LA-MRSA
- Feeding with tetracycline increase the load of MRSA in pigs
- MRSA transmission is also seen in antibiotic free conditions!

### - Heavy metals Zink, copper, cadmium, arsunate

- *crzC* is situated in *SCCmec 5C5&2c*

### - Pets? Rodents?

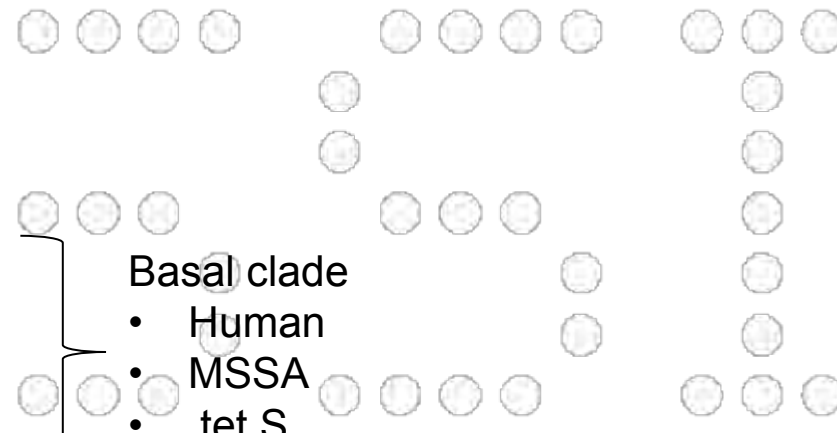
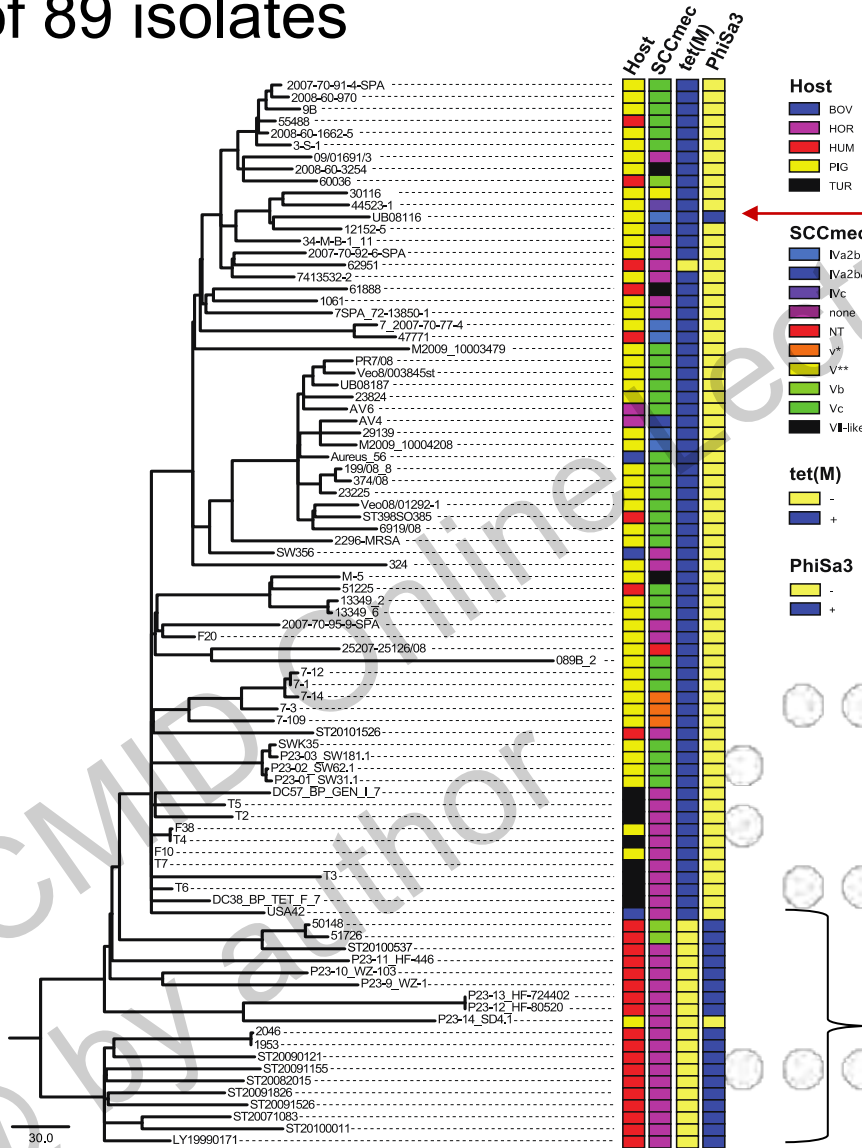
- ❖ Repeated contact with live positive animals
  - Exposure time
  - Type of animals
    - pigs and veal calves > chicken/turkey > dairy cows
    - Ecologic/antibiotic free farms vs conventional farms?
  - Repeated contamination vs colonization
  - However exposure is not equal to carriage
    - Vet students lost MRSA within 24 timer in a Dutch study
    - Prevalence in farmers drops after vacation / empty barn periods
  
- ❖ The risk for becoming a carrier is very low after a single short-time exposure



- ❖ Found in meat both from Denmark and several countries (at least from 2007 and onwards)
  - 5-20% of samples of pork
  - 20% of poultry
- ❖ As a consequence millions of people have handled meat throughout the period, however very few cases in large cities both in Denmark and in other countries
- ❖ Furthermore, workers at slaughterhouses working with meat only is very seldom positive
  
- ❖ Risk assesment: (Denmark and EFSA)
  - Risk is very limited for transmission through meat – the risk is associated to handling of the meat
    - Normal good kitchen hygiene including handwash after touching the meat will eliminate the risk

# RISK FOR ADAPTATION

## WGS of 89 isolates

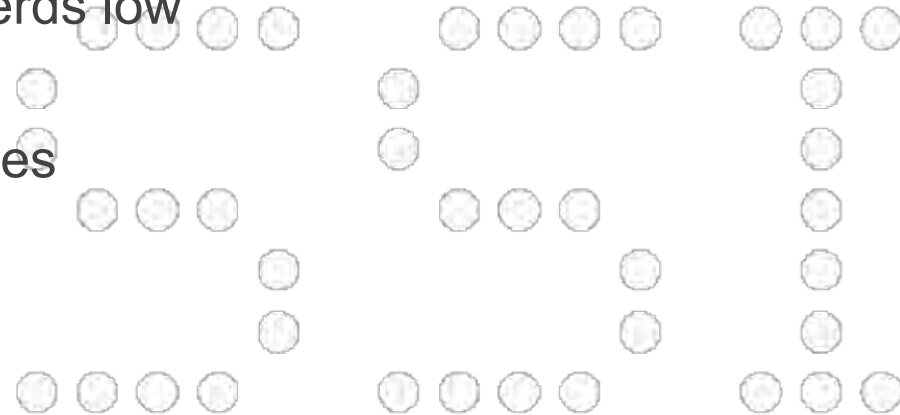


- Basal clade
- Human
  - MSSA
  - tet S
  - phiSa3

Price, mbio, 2012

- ❖ CA-MRSA is a separate entity – although not with a simple clear definition
- ❖ The prevalence of CA-MRSA is increasing worldwide and has moved from being a problem in closed risk communities to disseminate into the general population
- ❖ The boundary between HA-MRSA and CA-MRSA is getting increasingly blurred
- ❖ In some countries i.e. USA, Taiwan and Greece CA-MRSA strain types causes a significant portion of HAI
- ❖ LA-MRSA – a zoonosis which may change into a “community associated” MRSA i.e. with wide dissemination in the generalized population

- ❖ Both CA-MRSA and LA-MRSA must be taken seriously and should be suppressed by active plans of action
  - To avoid increasing prevalence of healthy carriers of MRSA which may threaten control of MRSA in hospitals
  
- ❖ Countermeasures against CA-MRSA can include
  - Admission screening
  - Decolonization treatment
  
- ❖ For LA-MRSA keep level of infected herds low
  - Low antibiotic usage
  - Keep the LA-MRSA within the stables
    - Hygiene precautions



THANK YOU FOR THE  
ATTENTION

