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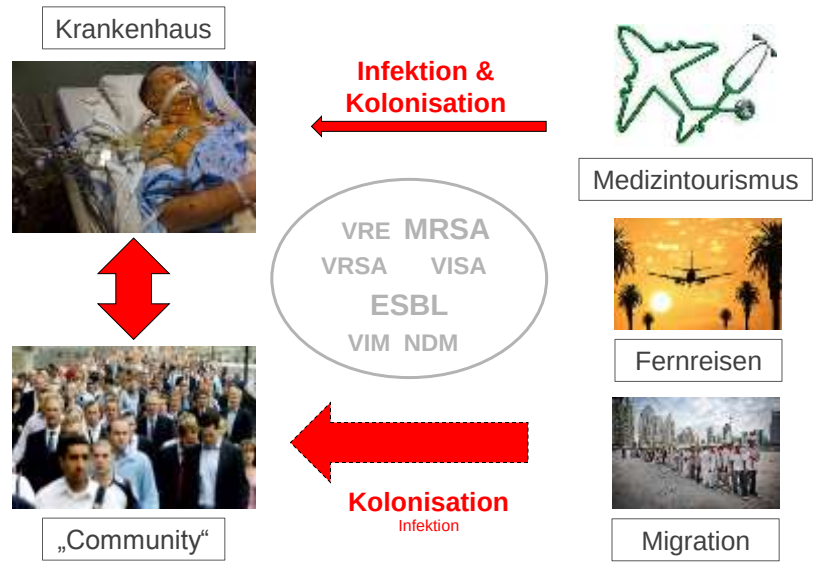
Antimikrobielle Resistenz und Migration

Philipp Zanger
Institute of Public Health, Heidelberg

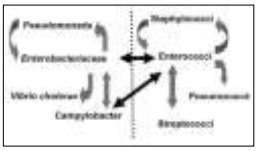
UniversityHospital Heidelberg

Bakterielle (Multi-)Resistenz und Migration

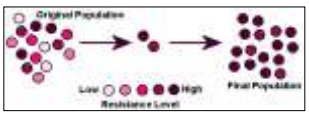


Die Entstehung globaler Resistenz

1. Veränderung des Genoms
- Spontane Mutation (selten)
- Austausch mobiler Elemente



2. Vermehrung durch Selektion
- "Survival of the fittest"



3. Ausbreitung über weite Entfernungen
- 1 Mrd. Flugreisende / Jahr
- Durchmischung von Populationen

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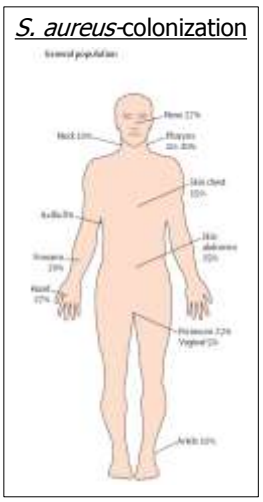
Kolonisierung mit potentiellen Pathogenen

- ***S. aureus***
- ***E. coli***
- ***Klebsiella spp.***
- *Pseudomonas aeruginosa*
- *S. pneumoniae*
- *Neisseria meningitidis*
- etc.



Wertheim, Lancet Infect Dis 2005

Die Ausbreitung von Resistenz: Die basale Reproduktionsrate (R_0)

$$R_0 = C * P * D$$

C = the number of contacts per unit time
P = the probability of transmission per contact
D = the duration of infectiousness

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Forschungsbedarf

Risikofaktoren

- gezielter Einsatz von Kontrollmaßnahmen

Geographische Verteilung von Resistenzmustern

- Grundlage empirischer Therapie

Prävention

- allgemeine / spezifische Prophylaxe

Surveillance

- neue Resistenzmuster

Fernreisen und Import von

Methicillin-resistentem *Staphylococcus aureus*

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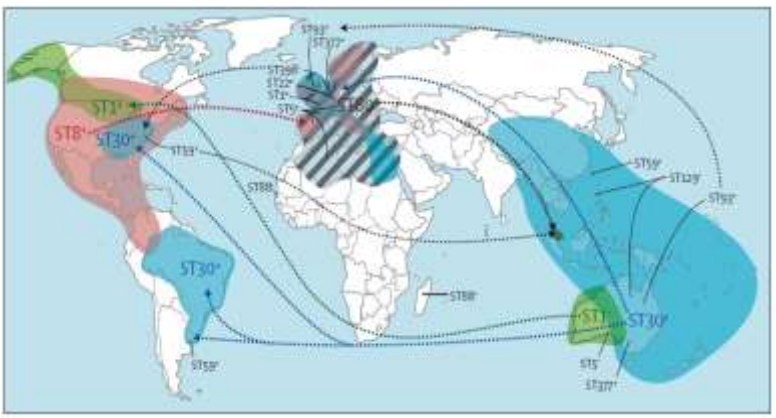
CA-MRSA: Molekulare Epidemiologie



•DeLeo, Lancet 2010

Regional unterschiedliches MRSA Risiko

MRSA Import nach Schweden (N= 267)
[50% Kolonisation, 50% Infektion]
[33% community-,66% hospital-acquired]

Country	IR / 1.000.000	OR adj.	95% CI
Nordic	0.1	**0.1**	0.01-0.6
Western Europe	0.9	**1.0**	-
North America	10.4	**10.6**	4.2-26.7
South America	39.5	**31.2**	10.0-97.6
East Asia	33.3	**36.5**	16.2-82.0
Oceania / Pacific	44.0	**43.0**	15.5-119.4
Sub-Saharan Africa	47.4	**46.3**	17.3-123.6
North-Africa / Middle East	59.4	**59.0**	25.1-138.9
Overall	**5.8 (5.2-6.6)**		

Stenhem et al., EID 2010

Risiko einer PVL+ *S. aureus* Infektion bei Reisen in die Tropen

Characteristic	*S. aureus* positive SSTI n=38	Control patients[a] n=124	Crude OR[b] (95% CI)	P-value[b]
Mean travel duration in months as natural log (SD)	0.84 (1.2)	0.31 (0.9)	1.6 (1.1-2.5)	0.02
Travel Destination				
East Asia	7 (18)	56 (45)	0.3 (0.1-0.7)	0.01
Latin America	6 (16)	34 (27)	0.5 (0.2-1.3)	0.2
Africa	18 (47)	27 (22)	3.2 (1.4-7.5)	0.006
Middle East/Central Asia	2 (5)	2 (2)	3.4 (0.5-25.3)	0.2
Australia/Pacific	5 (13)	5 (4)	3.6 (1.0-13.4)	0.06
Purpose of travel (ordered)				
educational	4 (11)	28 (23)[c]		
business	3 (8)	13 (11)[c]		
leisure	19 (50)	67 (54)[c]	1.7 (1.2-2.5)[c]	0.006
VFR	3 (8)	9 (7)[c]		
volunteering / humanitarian	9 (24)	6 (5)[c]		

Zanger et al. CID 2012

Weitere Risikofaktoren

- PVL assoziiert mit sekundärer Übertragung
- geliehene Tauchausrüstung
- Kontaktsportarten
- Gesundheitswesen
  - ICU, Aufenthaltsdauer, Antibiotika
- Ausbruchsereignisse in Krankenhäusern (Fallberichte)
  - erkrankter Reiserückkehrer
  - besiedeltes Krankenhauspersonal nach Urlaubsreise !!!

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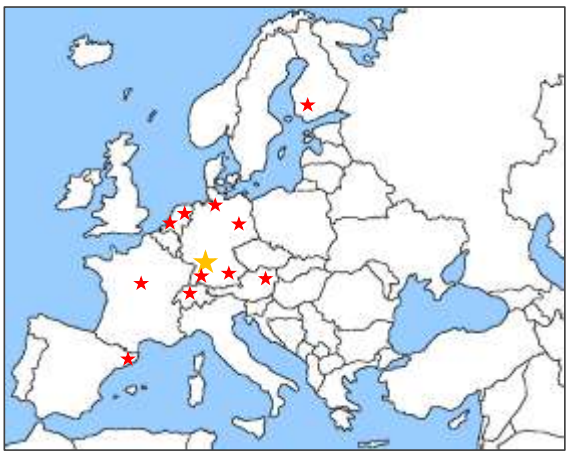
StaphTrav –European Network on Imported *S. aureus*



Submitting centers

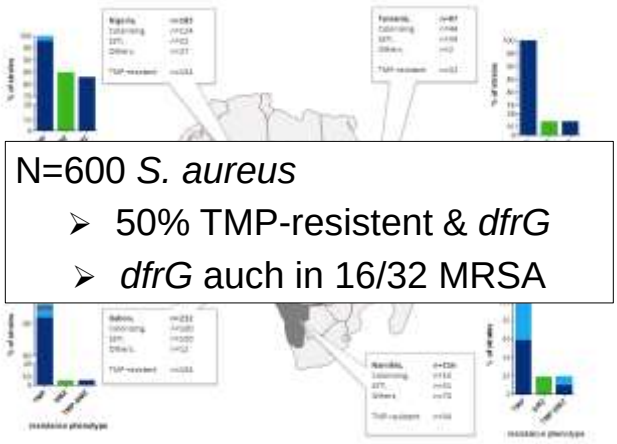
TMP-Resistenz bei Reiserückkehrern mit SSTI aus Afrika

Region	No. of strains	TMP	
		I	R
Southern Africa†	4	0	1 (25%)
West Africa‡	15	0	11 (73%)
East Africa§	21	0	10 (48%)
Central Africa¶	7	0	5 (71%)
Total	47		27 (57%)
Pre-travel subjects#	81	0	0

100% dfrG

Nurjadi et al. (accepted for publication)

TMP-resistance in *S. aureus* from Africa



N=600 *S. aureus*

- 50% TMP-resistent & *dfrG*
- *dfrG* auch in 16/32 MRSA

Nurjadi et al. (accepted for publication)

Fernreisen und Import von

ESBL

Multiresistenten gram-neagtiven Bakterien

Extended spectrum ß-lactamases (ESBL)

- **Genetic determinants**
  - TEM/SHV: Plasmid encoded
  - CTX-M: Plasmid encoded, from *Kluyvera* spp.
  - OXA: Plasmid encoded
  - KPC: Plasmid encoded
  - VIM / IMP: Plasmid encoded
  - NDM-1: Plasmid encoded

Carbapenemases

Metallo-

CTX-M-15 encoded ESBL in Europe

- “community onset infections”
- Zunehmend HWI durch **CTX-M-15** positive, pandemic ***E.coli*** **(ST131)**
- kombiniert mit Resistenz für TMP-SMX & FQ

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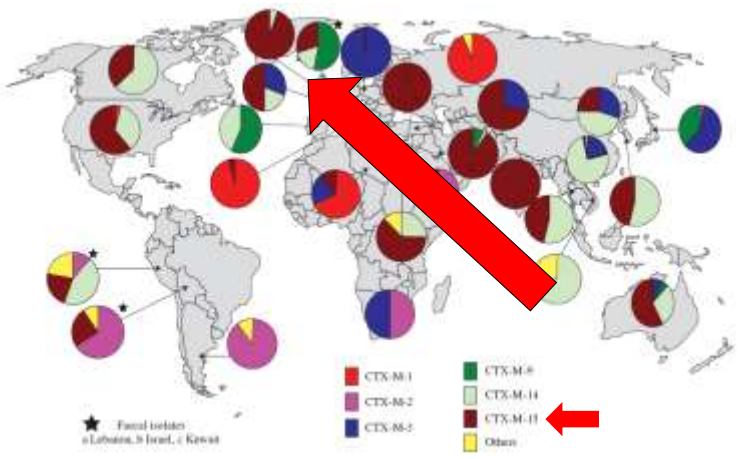
Global distribution of CTX-M-type ESBL



Hawkey, JAC 2009

RESEARCH NOTE

Extended spectrum β-lactamase-producing *Escherichia coli* faecal carriage in Spanish travellers returning from tropical and subtropical countries

in stool samples from 457 patients with travellers' diarrhoea who had travelled to tropical and subtropical countries. Ninety-seven ESBL-producing *E. coli* strains were isolated from 17.9% of the patients (82/457). CTX-M-15 was the most prevalent enzyme (80%) and India was the most visited country and showed the highest prevalence of positive samples (37.4%).

Solé, CMI 2014

Travel & ESBL

Foreign Travel Is a Major Risk Factor for Colonization with *Escherichia coli* Producing CTX-M-Type Extended-Spectrum β-Lactamases: a Prospective Study with Swedish Volunteers▽

Thomas Tängdén,[1]* Otto Cars,[1] Åsa Melhus,[2]† and Elisabeth Löwdin[1]†

Persistent colonization in 25% after 6 months !

Africa	25	1 (4)
Asia (India excluded)	31	10 (32)
Central America	6	0 (0)
India	8	7 (88)
Middle East	14	4 (29)
North America	2	0 (0)
South America	1	0 (0)
Southern Europe	16	2 (13)

* The rate of acquisition of ESBL-producing strains was highest for travelers visiting India ($P < 0.001$). Three participants visited more than one continent, and therefore, the sum of travelers in this table exceeds the actual number of 100.

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Travel & ESBL

TABLE 2. Distribution of CTX-M genes detected in 24 strains of *Escherichia coli* isolated from rectal swabs after foreign travel[a]

Continent or region	No. of isolates				
	Group I		Group IV		
	CTX-M-1	CTX-M-15	CTX-M-9	CTX-M-14	CTX-M-27
Africa		1			
Asia (India excluded)		2	1	5	2
India		7			
Southern Europe	1	1			
Middle East		2	2		
Total	1	13	3	5	2

Travel & ESBL

Community-onset extended-spectrum β-lactamase (ESBL) producing *Escherichia coli*: Importance of international travel

K.B. Laupland et al.

Table 1 Risk factors for development of community-onset ESBL-producing *Escherichia coli* infections among residents of the Calgary Health Region

Factor	Age Group	Number of cases/Total (%)	Relative Risk (95% Confidence Interval)[a]	p-value[b]
Hemodialysis	>19 yrs	4/146 (3)	56.3 (15.1–147.4)	<0.0001
Incontinence	>12 yrs	46/150 (31)	21.7 (15.0–30.9)	<0.0001
Cancer	>12 yrs	27/146 (18)	11.1 (7.0–17.0)	<0.0001
Ulcerative colitis	All	2/163 (1)	6.7 (0.8–24.6)	0.041
Overseas travel	All	71/163 (44)	5.7 (4.1–7.8)	<0.0001
India	All	14/163 (9)	145.6 (77.7–252.1)	<0.0001
Middle East	All	9/163 (6)	18.1 (8.1–35.2)	<0.0001
Africa	All	5/163 (3)	7.5 (2.8–17.2)	0.0002
South America	All	4/163 (2)	3.5 (1.0–9.2)	0.035
Asia[c]	All	22/163 (13)	3.4 (2.1–5.4)	<0.0001
Mexico	All	13/163 (8)	2.1 (1.1–3.7)	0.020
Heart disease	>12 yrs	32/150 (21)	6.5 (4.3–9.7)	<0.0001
Diabetes	>12 yrs	19/150 (13)	4.4 (2.6–7.1)	<0.0001
Chronic lung disease	>12 yrs	9/150 (6)	2.1 (0.9–4.0)	0.053
Smoker	>12 yrs	15/150 (10)	0.5 (0.2–0.8)	0.001

[a] Estimated 95% confidence intervals.
[b] Exact p-values; as a result, in some cases confidence limits include 1 despite a p-value less than 0.05.
[c] Excluding India and Middle Eastern countries.

Journal of Infection (2008) 57, 441–448

Zusammenfassung

- **Reisen trägt zu Verbreitung von Resistenz bei**
- **Grobe geographische Muster sind erkennbar**
  - MRSA USA/300 ST-8 aus Mittel- und Südamerika
  - *E. coli* CTX-M15 aus Indien
- **Evidenz zu anderen Risikofaktoren gemischt**
  - Reisegrund, -dauer
  - Aktivität am Zielort
- **Wenig Kenntnis** zum Umfang der Einschleppung in die Allgemeinbevölkerung
- **Weitere Forschung zu** Risikofaktoren, Impact, Kontrolle, und Prävention notwendig