

Temporary expert guidance for healthcare institutions to contain the spread of vancomycin-resistant enterococci (VRE) in Switzerland

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Introduction

Current situation

Vancomycin-resistant enterococci (VRE) are becoming a major concern for Swiss healthcare institutions with highly specialized care. Treatment options are limited because of multi-drug resistance. Over the last eight years large VRE outbreaks have occurred in Switzerland, mainly in the Canton of Vaud and most recently in the Canton of Bern with intra- and intercantonal spread to other hospitals. Despite its low pathogenicity, people at risk for serious infections (e.g. intra-abdominal infection, blood stream infections) are critically ill patients and those with a compromised immune system (e.g. hemato-oncological patients).

Different molecular strains have been identified in Switzerland, mainly ST17, ST80 and ST117. In 2018, ST796 became the most prevalent, due to the outbreak in the Berne region. ST796 was first detected in Australia/New Zealand and to date Switzerland is the first European country affected by this strain ([Wassilew et al. EuroSurv 2018](#)). It is characterized by rapid spread, potentially enhanced environmental survival, tolerance to low concentrations of alcohol and the ability to cause invasive infections in vulnerable patients.

According to a recent national survey (205 hospitals, 70% response rate), the yearly incidence increased from 96 VRE cases in 2015 to 146 cases in the first 3 months of 2018, corresponding to an increase in the rate from 0.26 cases/day in 2015 to 1.58 cases/day in 2018. Overall, 5 of 23 reported VRE outbreaks were observed between January 2018 and April 2018. Of these, four were ongoing at survey closure and 2/3 of these outbreaks experienced more than 5 cases.

At present, the VRE task force considers the following hospitals of the **Canton of Bern (Inselspital, Tiefenauhospital, Rehabilitation Clinic Belp, Spitalzentrum Biel)** as involved in the VRE outbreak. However, this list is incomplete and will need to be regularly revised and updated. Other cantons in the German-speaking parts of Switzerland (e.g. Aargau, Zurich, Basel) have recently observed an increase in the number of VRE cases requiring increased awareness.

Until further notice, we strongly recommend hospitals to be alert when receiving patients from other Swiss hospitals and to follow the recommendations as outlined below. For hospitals already experiencing a VRE outbreak a special section is included in the document.

Supported by the Swiss Federal Office of Public Health (FOPH) and Swissnoso, the VRE task force asks all hospitals and other healthcare institutions for a concerted action to combat the countrywide spread of VRE.

Importantly, the current guidelines are based on a consensus of a national expert group coordinated by Swissnoso and follow closely the recommendations issues by French and Vaud health authorities that proved successful in multiple instances over the last 15 years. Indeed, France and the French-speaking part of Switzerland have contained VRE transmission at a large scale.

In contrast, the soon to be released German recommendations are minimalistic (“Schadensbegrenzung”) and adopted for a country with already hyperendemic spread of VRE (incl. even linezolid-resistant VRE) across the entire country. Thus, we caution our Swiss colleagues not to follow German VRE control guidelines in the near future. We should use this time window for action before the wave of VRE makes interventions extremely expensive and success not guaranteed.

The task force, however, recognizes that there might be particular situations and reasons in an individual hospital making deviations from these recommendations necessary. Such decisions should be discussed with the local infection prevention and control team.

Aims of this expert guidance document

- To contain the ongoing spread of VRE within and between health-care institutions
- To interrupt intra- and intercantonal VRE transmission
- To update hospital hygienists and infectious disease specialists on the core elements of successful VRE control

The core principles of VRE containment

A successful VRE containment strategy includes the following crucial elements:

1) The iceberg tip principle

Since the ratio colonization/infection is greatly unbalanced ($>1/10$), the first isolation of VRE in a clinical sample strongly suggests undetected VRE carriage

2) The onion skin principle

Detection of a VRE case should trigger screening of all contact patients according to a strategy of concentric circles

3) The Speedy Gonzales principle

Rapidity of detection and isolation of VRE patients and contacts is probably the most critical point

Target groups of these recommendations

This document is intended for nurses, physicians and infection prevention and control (IPC) teams in acute care settings. For healthcare institutions outside the acute care setting (e.g., rehabilitation/long term care facilities) we recommend to reinforce standard precautions for all patients and to implement additional precaution measures based on individual risk assessment. Importantly, the wellbeing of patients that are positive for multidrug resistant bacteria including VRE should not be further compromised and, therefore, these facilities should normally accept such patients and offer them participation on activities equal to other patients.

Mode of transmission

Enterococci are mostly transmitted by contact (droplets if airways are colonized or infected). Main vectors of transmission in the hospital setting are the hands of healthcare workers but enterococci are also able to survive on inanimate surfaces for prolonged periods of time and environment can therefore be a persistent source. Even after thorough cleaning and high-level disinfection, VRE is detectable on surfaces after 3-4 hours, in particular, when a VRE patient is close or even in the room.

Definitions

Outbreak

- ≥ 3 VRE cases with a possible epidemiological link on ward or institution level

VRE case

- Patient with a positive culture (clinical or screening sample) for *E. faecium* being resistant to amoxicillin and vancomycin (confirmed by pheno- or genotype).

VRE contact

- Patient is or has been hospitalized (going back to the entire stay of the index patient but max. 30 days) in the same room with a VRE patient

OR

- Patient on a ward where a VRE outbreak has been documented

Possible VRE contact

- Patient from a hospital in Switzerland with known VRE outbreaks but not fulfilling the criteria above
- Patient transferred from a hospital outside Switzerland with a hospital stay of > 24 hours

NOTE:

- a) Definitions of “VRE contact” and “possible VRE contact”, respectively, apply to all those without a complete set of negative screening results (see screening for VRE below) and should also be considered in already discharged patients.
- b) **Countries with high VRE prevalence in Europe** currently concern in particular: Germany, Italy, United Kingdom, Bulgaria, Croatia, Hungary, Poland, Romania, Portugal, Ireland, Cyprus and Greece. Outside Europe, it concerns mainly North America, Australia and New Zealand

(Pre-emptive) contact precautions (CP)

Indication

- Strictly enforced CP: all identified VRE cases
- Pre-emptive CP: VRE contacts (if feasible, it is highly recommended, otherwise standard precautions as for *possible* VRE contacts, especially reinforce hand hygiene compliance and environmental cleaning)

Implementation

- CP according to local guidelines, which should include ideally
 - o single room with own washroom/toilet
 - o daily cleaning/disinfection of the room (and, at the end of the hospital stay, terminal room disinfection)
 - o prefer single use items or dedicated equipment
 - o every item that is removed from the room needs to be disinfected
 - o secured elimination of excreta (use washer disinfector for stool basins and strict hand hygiene)

Discontinuation of (pre-emptive) CP

VRE cases

- VRE colonization may persist up to several months to years depending on the presence of risk factors
- Earliest termination of CP possible after a minimum of 3 consecutive negative rectal swabs of high quality (visible fecal material, otherwise obtain stool culture) collected

over one month (at least 4 weeks between the first and the last negative swab) provided that any other body site previously infected or colonized by VRE (e.g. urine or wounds) is also found negative.

- Five negative high-quality rectal swabs each one week apart are recommended in case of an ongoing VRE outbreak.

NOTE:

- a) For VRE cases with 3 consecutive negative swabs we highly recommend to repeat screening after 6 months and to require another series of 3 consecutive negative screenings before declaring a patient completely free from VRE.
- b) Hospitals may also consider extending CP (e.g. for 6 months) prior to assessing the discontinuation of CP in patients at risk for prolonged carriage: e.g. highly immunosuppressed, receiving broad spectrum systemic antimicrobial therapy without VRE activity (e.g. cephalosporins), receiving care in protected environments or receiving care at institutions with high ($\geq 10\%$) or increasing rates of VRE infection

VRE contacts

- Earliest termination of preemptive CP if three consecutive negative screenings have been retrieved (e.g. days 0, 7, and 14 after last exposure)

Screening for VRE

Indication

Mandatory screening

1. All patients at high risk for VRE carriage, eg. direct contacts of newly identified VRE index patients
2. Readmitted patients previously known to be VRE carriers
3. Patients transferred from hospitals in the Bern region or other regions with epidemic occurrence of VRE (**information to be updated regularly by Swissnoso and Anresis: www.swissnoso.ch**)
4. All patients directly transferred from a hospital outside Switzerland irrespective of the country of origin (for this patient group screening for carbapenemase- and ESBL-producing Enterobacteriaceae, and MRSA is also highly recommended). In particular, we highlight the importance to screen all patients transferred from German healthcare institutions for asymptomatic VRE carriage.

Optional screening

1. Some Swiss healthcare institutions may decide to screen for VRE all patients transferred from any healthcare institution in Switzerland, irrespective of the canton of origin. This policy should be strongly considered for highly specialized acute care units such as: transplant units, neonatal and adult intensive care units, hemodialysis units, and oncology-hematology units.
2. Patients with a previous hospital stay > 24 hours outside Switzerland within the last 12 months but not directly transferred (for this patient group screening for carbapenemases-producing, ESBL-producing Enterobacteriaceae, and MRSA is also highly recommended; if this policy is already implemented in your hospital, the expert group suggests adding VRE to the screening panel of multidrug-resistant bacteria)
3. Patients admitted to high-risk units (e.g., bone marrow transplant [BMT] or hemodialysis unit)
4. Patients included in targeted prevalence surveys according to local epidemiologic considerations and needs (e.g., weekly or monthly prevalence surveys in ICUs or BMT units)

NOTE:

As one clinical sample (e.g., urine, blood culture) positive for VRE can be the first signal of a silent VRE transmission within an institution, an investigation around such a case should always be performed (screening of roommates since admission +/- patients hospitalized in the same ward at present).

Methods

- **Rectal swab** (insert the swab about 4 cm into the rectum, gently move the swab in a circle 2 or 3 times, touching the walls of the rectum, **visible fecal material required**).
- A stool culture searching for VRE may also be performed if a high-quality rectal swab cannot be obtained. However, time may pass as a fecal specimen may take days to get to the laboratory.
- Consider additional urine culture when catheter in place
- Consider additional swab of open wounds
- Type of swab and tubes according to local laboratory guidelines
- Immediate processing of the swabs in a clinical microbiological laboratory recommended (storage at 4°C for 24-72 hours before processing is possible)

Number of swabs for screening:

VRE contact

- At least three separate cultures on days 0, 7 and 14 after last exposure is highly recommended

Possible VRE contact

- At least one screening on admission

Healthcare institutions with recent or ongoing VRE outbreaks/clusters

General measures

- Form an outbreak management team with the following suggested members: clinical microbiologist, one or more infection control specialists, a member of the hospital management team, a representative from the medical staff (e.g., nursing leadership), a representative of the hospital communication team, and a manager of housekeeping and logistics
- Limit patient transfer to other wards, departments and other hospitals if not absolutely required
- Maintain high compliance with standard precautions (hand hygiene, wearing gowns, gloves and/or masks if contact or splashes with body fluids is anticipated, respiratory etiquette) in all patients
- Place VRE cases under CP and VRE contacts under preemptive CP, implement cohorting for VRE cases if possible (for definitions of VRE cases and VRE contacts and for recommendations on CP duration please see above)
- Label patients (electronically, patient management system)
- Systematic screening by rectal swab: screen all patients on hospital wards at the beginning of an outbreak or on wards with ongoing VRE transmissions (once a week or at least on admission and at discharge)
- Daily cleaning and disinfection of rooms with patients positive for VRE (once or twice a day plus at discharge)

Extended measures depending on size of outbreak

Evaluate further measures depending on size of outbreak and according to available resources:

- Enhance further actions to increase awareness of standard hygiene measures
- Organize 3 dedicated zones or wards with dedicated staff (“cohorting”) for each zone, if feasible:
 1. ‘VRE’ zone/ward: accommodate VRE cases
 2. ‘Contact’ zone/ward: accommodate all contact patients without a complete set of negative screening results.
 3. ‘Clear’ zone/wards: Patients who were not contacts or had not been previously admitted to the hospital during the outbreak
- Organize dedicated staff
- Non-ward staff (e.g. physiotherapist, nutritional specialist, medical doctors from other disciplines etc.) are asked to re-group their patient sessions/consultations to avoid multiple entries into the VRE zone/ward
- Consider restriction of antibiotic classes (e.g. oral vancomycin, cephalosporins, relinquish ciprofloxacin prophylaxis during neutropenia)
- Consider environmental cultures of frequently touched surfaces (e.g. bed rails, light switch) and high-risk items, in particular toilets.
- Evaluate the possibility to use no-touch disinfection methods (e.g. hydrogen peroxide vapor or UV-C light) for rooms of VRE-positive patients after discharge and/or closed wards before reopening them for other (non-VRE) patients (before using hydrogen peroxide vapor the room or ward needs to be completely sealed)
- Consider admission stop of newly admitted patients to the concerned unit early on
- Consider using antiseptic body washes with $\geq 2\%$ chlorhexidine gluconate in patients at high risk of invasive VRE infections (e.g. those with a central venous catheter)
- Staff screening is not recommended.

Referring patients to other healthcare institutions

- Ideally, patients should be screened for VRE before referral to another healthcare institution.

- If screening could not be performed, the receiving institution should be notified in advance about the VRE situation in the referring hospital (see Definitions above) so that screening measures can be performed promptly upon admission
- The responsible physician and/or ward nurse and the infection control nurse have to inform the health-care workers (ward nurse, infection control nurse or physician, respectively) of the designated healthcare institution by phone and by writing a note in the (preliminary) discharge letter whether the patient is:
 - o VRE positive (**VRE case**) or under investigation for VRE carriage (**VRE contact**) and
 - o had rectal screenings (date and results) before discharge or transfer

Communication/information

- Inform involved responsible nurses/physicians of wards and departments, CEO/director, communication, according internal outbreak- and communication-guidelines
- Inform involved patients and their families
- Label VRE cases and VRE contacts clearly visible in the patient file or nursing chart

Mandatory notification

- Report an outbreak to your cantonal physician as “Häufung von klinischen oder laboranalytischen Befunden” (Meldeformular BAG: Häufung von Beobachtungen)
- For the current moment, Swissnoso recommends that institutions follow a pragmatic approach and notify twice:
 - a. Report at the beginning (as soon as possible): if ≥ 3 VRE cases are identified
 - b. Report if the outbreak is terminated (with the total number of identified VRE cases)
- Cantonal physicians transmit these notifications as all others to the FOPH

Healthcare institutions receiving patients from institutions with recent or ongoing VRE outbreaks/clusters

Measures

- Label VRE cases and VRE contacts clearly visible in the patient file or nursing chart wherever possible for VRE-screening/contact precautions
- Place VRE cases under CP and VRE contacts under pre-emptive CP (see under: Indication)

- Screening for VRE: initiate/complete VRE-screening (see under: **Screening for VRE**)
- Apply standard precautions on all other transferred patients and consider VRE-screening for **Possible VRE contacts** (see **Definitions** and **Screening for VRE** above)
- Try to identify patients formerly transferred from outbreak hospitals in the Bern region or other affected hospitals since 01.01.2018 (check with patient administration or controlling department) and also label them for VRE-screening/contact precaution

Communication/information

- Inform responsible departments according to the local situation (emergency department, intensive care units, hospital director/CEO, ...)
- Contact infection prevention and control team of outbreak hospitals for further information of (previously) transferred patients regarding risk of VRE exposure, initiated VRE screening, available screening results, etc. highly recommended

Microbiology

- (Pre-) inform your laboratory about the local situation (epidemiology, planned screening) and coordinate any control measures with the microbiology laboratory

Microbiological confirmation of VRE

- VRE are enterococci with minimum inhibitory concentrations (MIC) to vancomycin of $\geq 4\text{mg/mL}$ or zone diameter breakpoint $< 12\text{ mm}$ (according to EUCAST v8.1 guidelines)
- Test for teicoplanin MICs to already establish the phenotype that could eventually correspond to the vanA or vanB genotypes (susceptibility to teicoplanin may be variable according to the genetic background of the involved VRE clone: vanA strain, mostly teicoplanin-resistant; vanB, mostly teicoplanin-susceptible)
- Perform confirmatory PCR testing for vanA and vanB genes if available in house or send the strain to a laboratory with available testing methods
- Laboratories can also contact NARA for further support (Nationales Referenzlaboratorium zur Früherkennung neuer Antibiotikaresistenzen und Resistenzmechanismen; www.nara-antibiotic-resistance.ch/fr/fiches_techniques/)
- Whole genome sequencing based typing of VRE isolates is recommended in case of outbreaks and for specific patient populations; thus, strains should be stored for later molecular analyses (for contact details please see below).

Laboratories with capacity and expertise in whole genome sequencing of VRE:

**Universitätsspital Basel
Klinische Mikrobiologie**

Petersgraben 4

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Summary of recommended measures to be implemented in the endemic and outbreak setting to contain the spread of vancomycin resistant enterococci (VRE)

	Healthcare institutions receiving patients from hospitals with VRE clusters or outbreaks	Hospitals with a VRE cluster or an ongoing outbreak (≥ 3 cases)
Standard precautions (all patients)	<ul style="list-style-type: none"> Reinforce standard precautions, especially hand hygiene, wearing gloves, gowns and/or masks if contact or splashes with bodily fluid is anticipated 	<ul style="list-style-type: none"> Reinforce standard precautions, especially hand hygiene, wearing gloves, gowns and/or masks if contact or splashes with bodily fluid is anticipated
Contact precautions (CP) (VRE cases/contacts)	<ul style="list-style-type: none"> CP according to local guidelines: <ul style="list-style-type: none"> Single room with own toilet Dedicated equipment Clearly label the room of a patient in contact precaution 	<ul style="list-style-type: none"> CP according to local guidelines <ul style="list-style-type: none"> Single room with own toilet Dedicated equipment Cohorting possible Clearly label the room/zone of patients in contact precaution
(Electronic) labeling (VRE cases/contacts)	<ul style="list-style-type: none"> Label VRE cases and VRE contacts in the patient file and/or nursing chart 	<ul style="list-style-type: none"> Label VRE cases and VRE contacts in the patient file and/or nursing chart
Mandatory VRE screening	<ol style="list-style-type: none"> All patients at high risk for VRE carriage, eg. direct contacts of VRE index patients Readmitted patients previously known to be VRE carriers Patients transferred from hospitals in the Berne region or other regions with epidemic occurrence of VRE (information to be updated regularly by Swissnoso and Anresis) Patients directly transferred from a hospital outside Switzerland 	
Optional VRE screening	<ol style="list-style-type: none"> All patients transferred from any healthcare institution in Switzerland (to be strongly considered for highly specialized acute care units). Patients with a previous hospital stay > 24 hours outside Switzerland within the last 12 months but not directly transferred Patients admitted to high-risk units (e.g. BMT or hemodialysis unit) Patients included in targeted prevalence surveys according to local epidemiologic considerations and needs (eg. weekly or monthly prevalence surveys in ICUs, hemodialysis or BMT units) 	
Number of screenings	<ul style="list-style-type: none"> VRE contact: at least 3 rectal swabs (visible fecal material) on a weekly basis (day 0, 7, and 14 after last exposure) possible VRE contact: at least 1 rectal swab 	
Ward organization	<ul style="list-style-type: none"> Ward rounds: start with non-VRE patients first and visit VRE-case last 	<ul style="list-style-type: none"> Consider ward closure/admission stop to a concerned unit early on Organize 3 dedicated zones/units: <ul style="list-style-type: none"> VRE zone/unit Contact zone/unit Clear zone/unit Each zone with separate toilets Each zone with dedicated staff Ward rounds/other personnel entering the ward: visit patients in clear zone first and end with VRE zone
Patient flow (VRE cases/contacts)	<ul style="list-style-type: none"> Limit patient transfers if not absolutely required 	<ul style="list-style-type: none"> Limit patient transfers if not absolutely required in case of transfer: notify receiving institution in advance of the VRE situation in the discharge hospital
Environmental decontamination (VRE cases/contacts)	<ul style="list-style-type: none"> Daily cleaning & disinfection Terminal room disinfection 	<ul style="list-style-type: none"> Once or twice daily cleaning & disinfection and terminal room disinfection Consider non-touch disinfection methods (hydrogen peroxide vapor, UV-light) for terminal room/ward disinfection
Communication/ information	<ul style="list-style-type: none"> Inform involved patients and their families 	<ul style="list-style-type: none"> Form an outbreak management team (multidisciplinary coordination)

	<ul style="list-style-type: none"> • Inform responsible departments according local situation • (pre-)inform your microbiology laboratory 	<ul style="list-style-type: none"> • Inform involved patients and their families • Inform responsible departments according local situation
Mandatory notification		<ul style="list-style-type: none"> • Notify the the cantonal physician by reporting "<i>Häufung von klinischen oder laboranalytischen Befunden</i>"
Further epidemiological investigations	<ul style="list-style-type: none"> • Identify and screen contacts of a new VRE case • Consider screening of all patients on a ward with a newly identified VRE case (remember: one clinical sample positive for VRE can be the first sign of an unperceived VRE transmission) 	<ul style="list-style-type: none"> • Identify and screen contacts of a new VRE case • Systematically screen all patients on hospital wards at the beginning of an outbreak or on wards with ongoing VRE transmissions (once a week or at least on admission and at discharge)
Environmental cultures		<ul style="list-style-type: none"> • Consider performing cultures of frequently touched surfaces (e.g. bed rails, light switch) and high-risk items
Antibiotic restriction	<ul style="list-style-type: none"> • Establish an antibiotic stewardship program if not already in place 	<ul style="list-style-type: none"> • Limit administration of oral vancomycin, consider penicillin alternatives for treatment with broad-spectrum cephalosporin, relinquish fluoroquinolone prophylaxis during neutropenia
Termination of CP	<ul style="list-style-type: none"> • VRE cases: at least 3 negative consecutive swabs of high quality (visible fecal material) taken over one month (at least 4 weeks between the first and the last swab , • provided any other site previously found infected or colonized by VRE (e.g. urine, wound) is also found negative • decide on a case by case basis (e.g. risk for prolonged carriage) 	<ul style="list-style-type: none"> • VRE cases: at least 5 negative consecutive swabs of high quality (visible fecal material) each taken 1 week apart • provided any other site previously found infected or colonized by VRE (e.g. urine, wound) is also found negative • decide on a case by case basis (e.g. risk for prolonged carriage) • if rates of VRE cases are increasing consider extension of CP
Termination of preemptive CP	<ul style="list-style-type: none"> • VRE contacts: at least 3 negative consecutive swabs of high quality (visible fecal material) on a weekly basis: <ul style="list-style-type: none"> ○ day 0, 7 and 14 after last exposure 	<ul style="list-style-type: none"> • VRE contacts: at least 3 negative consecutive swabs of high quality (visible fecal material) on a weekly basis: <ul style="list-style-type: none"> ○ day 0, 7 and 14 after last exposure • if rates of VRE cases are increasing consider extension of CP

(Adapted from Moulin E. et al. Rev Med Suisse 2018; 14 : 791-4 and based on French recommendations)

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VRE taskforce

The VRE taskforce is an *ad hoc* assembled group of national experts in the fields of infection prevention and control, microbiology, epidemiology and public health. Its members are representatives of the following organizations: Swissnoso, Swiss Society of Hospital Hygiene (SSHH), Swiss Society of Microbiology (SSM), Swiss Society of Infectious Diseases (SSI), Swiss Association of Cantonal Officers of Health (VKS-AMCS), and the Swiss Centre for Antibiotic Resistance (anresis.ch).

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