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# Swiss Centre for Antibiotic Resistance

## *Algorithms*

akm software / anresis.ch

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# 1 Algorithms in Resistance Database

## 1.1 Resistance Pattern

The resistance pattern of a sample microorganism is characterized by:

- the number of resistances against antibiotics
- the individual antibiotics, against which resistances were found
- the qualitative resistance of each individual antibiotic – The following table represents the rules for the comparison of two qualitative resistances:

| qualitative resistance of a sample microorganism from sample A against an antibiotic | qualitative resistance of a sample microorganism from sample B against an antibiotic | result |
|---|---|---|
| susceptible | susceptible | = |
| Susceptible | intermediate | = |
| Susceptible | resistant | ≠ |
| Resistant | intermediate | = |
| Resistant | resistant | = |
| Intermediate | intermediate | = |

Summary: Two qualitative resistances are unequal only in the case, that one of both is susceptible and the other is resistant. The value **intermediate** can be considered as "wild card".

## 1.2 Infection versus Colonisation

Colonisation means the natural presence of microorganisms on skin or mucous membranes (e.g. mouth, intestines etc.) without causing an infection. The colonisation property is assigned to the sample microorganism. Thus there is the possibility to exclude colonizing microorganisms from the analysis.

The kind of the calculation of this attribute depends on the sample type. The sample type is determined by the sample location.

**blood culture, catheter tip** (Katheterspitze) (SAMPLE_LOCATION_ORGAN = BLOOD)

For this case only sample microorganisms are considered, for which the attribute *relevant for colonisation/infection* of the corresponding microorganism is set to *true.* The criteria for an infection are:

- There is a double entry (see 3.6 and 3.2) to the sample microorganism within a determined period, e.g. the last seven days. The length of this period should be freely configurable. The period is defined by the difference of the *sampling dates* of the considered samples. If one or more sampling dates are missing, then the arrival dates will be used.
- The sample was taken from two or more blood cultures or from one blood culture and one ore more catheter apexes (Katheterspitzen).

**Urine** (SAMPLE_TYPE = urine)

For this case all sample microorganisms of the sample are considered. The criteria for an infection are:

- The number of sample microorganisms in the sample is less than three.
- The concentration of the corresponding sample microorganisms is equal to or greater than 10E5 per ml.

**respiratory**

For this case all sample microorganisms of the sample are considered. The criteria for an infection are:

- The number of sample microorganisms in the sample is less than three.
- The value for leukocytes in the sample is positive, i.e. the attribute *leukocytes* has the value *true*.
- The value for epithelial cells in the sample is negative, i.e. the attribute *epithelial cells* has the value *false*.
- The sample location acronym is “bal” or “tbs”.

**References:** Chapter 5.3.1.6 in **[1]**

## 1.3 “Possibly Nosocomial” vs. Ambulant

*Nosocomial* means that the patient obtained the microorganism within the hospital. In contrast to that *ambulant* means that the microorganism was obtained outside of the hospital.

A prerequisite for the determination of this property of a sample microorganism are two samples of a hospitalized patient. The attribute *hospitalization date* of the entity *sample* specifies whether the patient was hospitalized or not.

The attribute *possibly nosocomial* of a microorganism is set to *true*, if one of the following criteria is fulfilled:

1. The microorganism belongs to a sample which is taken more than two days after the hospitalization of the patient. The length of this period should be freely configurable. There is no sample taken within the first two days after the hospitalization with the same *patient id*, *laboratory id* and the *hospitalization date*.
2. The microorganism is *probably nosocomial*.

## 1.4 “Probably Nosocomial” vs. Ambulant

*Nosocomial* means that the patient obtained the microorganism within the hospital. In contrast to that *ambulant* means that the microorganism was obtained outside of the hospital.

A prerequisite for the determination of this property of a sample microorganism are two samples of a hospitalized patient. The attribute *hospitalization date* of the entity *sample* specifies whether the patient was hospitalized or not.

1. The first sample is taken within the first two days after the hospitalization of the patient. The length of this period, which should be freely configurable, is determined by the difference between the *sampling date* and the *hospitalization date*. If the sampling dates are not available, then the *arrival dates* should be used. One assumes that all microorganisms that were identified in this sample were obtained before the hospitalization. The attribute *probably nosocomial* is set to *false* for all sample microorganisms of the sample.
2. The second sample is taken more than two days after the hospitalization of the patient. The length of this period should be freely configurable. The relationship to the first sample is made by the *patient id*, *laboratory id* and the *hospitalization date*.
    - For each *sample microorganism* of the second sample, which is not contained in the first sample or has a different resistance pattern, the attribute *probably nosocomial* is set to *true*.
    - For all *sample microorganisms*, which were identified in both samples with the identical resistance pattern (see 3.2), the attribute *probably nosocomial* is set to false.

**References:** Chapter 5.3.1.5 in **[1]**

## 1.5 Double Entry resp. Repetition

A double entry is an identical microorganism, i.e. an identical resistance pattern, isolated from the same patient and from the same or a different anatomical site within a defined period.

There are three different situations that may lead to a double entry:

- additional analysis of one and the same sample through a reference center laboratory
- additional analysis of one and the same sample through a reference laboratory
- multiple samples from the same patient – Also sample microorganisms of different samples can be called double entries, if they have the same resistance pattern. A more correct name for this case would be *repetition*.

The first two cases can only be detected, if the laboratory which analyzed the sample provides this information.

The detection algorithm for the third case is described in the following. It is performed in 4 variations:

1. Double entries for period 1 for all sample location types.
2. Double entries for period 2 for all sample location types.
3. Double entries for period 1 with matching sample location types.
4. Double entries for period 2 with matching sample location types.

Period 1 (default 7 days) and period 2 (default 365 days) are freely configurable. Period 2 must not be shorter than period 1.

Two (ore more) samples are considered as double entries or repetition if:

- they belong to the same laboratory, i.e. they have a identical *laboratory id*
- they belong to the same patient, i.e. they have a identical *patient id*
- they were taken within a definite period (period 1 or period 2). The length of this period is defined by the difference of the corresponding *sampling dates.* In the case that the sampling dates are not available the *arrival dates* should be used.
- the resistance pattern (see 3.2) of a microorganism is identical in both samples

For variation 3 and 4 of the algorithm additionally the following must be the case for the samples:

- they belong have the same sample location type.

## 1.6 Qualitative Resistance (not implemented)

If it is possible, then the qualitative resistance is recalculated from the quantitative resistance. The recalculation of the qualitative resistance takes place, because the quantitative data, i.e. the raw data, have a higher priority than the qualitative resistance which is provided by the laboratory. A prerequisite for the calculation of the qualitative resistance is the supply of the quantitative data by the laboratory and the availability of the conversion rules/formulas (NCCLS, Steering Committee, ESBL test, ...).
**These conversion rules/formulas are currently not implemented.**

The priority of the quantitative data for the recalculation of the qualitative resistance is configurable.

# 2 Algorithms and episode handling in Bacteremia Database

During the data clearing process of resistance data SEARCH runs algorithms to

1. classify infection vs. contamination
2. classify nosocomial vs. ambulant.

***Important note:*** *The algorithms described in this chapter are not exactly the same as currently running in resistance database. It is one task of the Bacteremia subproject to adjust these algorithms as defined here.*

The infection algorithm relies on the determination of “doubles” resp. “repetitions” for resistance data (see chapter 1.5). For bacteremia data the interpretation of doubles is slightly different.

## 2.1 Doubles and episodes

For resistance data a **double** is defined as a repetition of microorganism occurrence with identical resistance pattern in two different samples within a given time period (e.g. 7 days).

For bacteremia data there are two main differences to this interpretation:

1. Resistance pattern is not taken into account for double comparison of two microorganisms.
2. In resistance data a sample microorganism is only marked as double if the same microorganism (including resistance pattern) is detected in another sample of the same patient and laboratory within a given time period (7 days or 365 days resp.). In bacteremia surveillance this interpretation is also needed for the infection algorithm. However, for analysis of bacteremia only “episodes” are counted. An episode is built from samples by the sequence of blood cultures or catheters taken in steps of maximum 7 days, regardless whether a microorganism could be detected or not.

In order to correctly count bacteremia occurrences, samples (from the same patient) taken within 7 days belong to the same episode, as long as any microorganism has been detected. An episode of samples ends as soon as the next MO-positive sample is more than 7 days after the last one, either because interjacent samples did not show microorganisms, or no sample has been taken during that period. A sequence of MO-negative samples build a sequence of distinct episodes, each counted separately, but with an exactly length of 7 days as long as no positive occurs.

Chapter 2.4 shall illustrate the building of episodes. It shows possible sequences of samples taken from the same patient at the same laboratory (either blood culture or catheter, treated as identical sample locations for episodes), where “+” denominates a positive growth of microorganism and “-” a negative result.

## 2.2 Infection vs. Contamination

The infection algorithm is based on detection of doubles. While determination of doubles slightly differs in resistance and bacteremia, once they are marked accordingly in resistance and bacteremia data, the infection algorithm shall be identical for both sets.

***Note**: In the current implementation of infection algorithm in resistance data Neonatology-ICU criterion is not regarded yet. The algorithm shall be adapted within bacteremia implementation.*

In order to describe the common algorithm we use the terms “double” as seen in 2.3.1 (which may be set different in resistance and bacteremia data) and “original”, meaning the first occurrence of a specific microorganism to which the doubles belong.

1. If the MO is not in the list of opportunistic microorganisms or if the speciality is “FMH Neonatologie” it is an **infection**.

2. Otherwise, if the MO is a double (or an original with existing doubles), all doubles and the original record are marked as **infection**.

3. Otherwise, the record is marked as **contamination**.

Remarks:

- Information about the site of blood culture (central or peripheral) does not enter this algorithm, since this information is often not available or incorrect.
- There is a need to check with all laboratories, that 1 blood culture is defined as a set of two bottles (e.g.g aerobic and anaerobic)
- For counting in analysis episodes have to be taken into account.

## 2.3 Nosocomial vs. Ambulant

The determination of nosocomial versus ambulant samples is handled in the same manner as in resistance data.

## 2.4 Examples of episodes

| Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | remarks |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1) | + | | | | + | | | | | + | | | | - | | | | | | | | | | | | | | | | | | | | | | | | | | One episode: all tests within 7 days, last result negative but part of this episode |
| 2) | + | | | | + | | | | | | | | | | + | | | | + | | | | | | | | | | | | | | | | | | | | Two different episodes as >7d between sample 2 and 3 |
| 3) | + | | | | + | | | | | + | | | | - | | | | + | | + | | + | | - | | | | | | | | | | | | | | Two different episodes. Sample on day 14 is negativ, sample on day 18 positive but last positive sample >7d before on day 10 |
| 4) | + | | | | + | | | | | + | | | | - | | | | - | - | - | | - | | - | | - | | - | | - | | | - | | | | | Three different episodes. The first episode ends on day 20, as a maximum of 7 days are allowed between first and last negative sample. The negative sample on day 30 starts a new episode, as the maximum length of a negative episode is defined as 7 days. |
| 5) | + | | | | + | | | | | + | | | | - | | | | - | | - | | - | | + | | + | | | + | | | - | | | | | | Three different episodes. The negative sample on day 22 builds a separate (negative) episode as the positive sample on day 24 starts a new (positive) episode. |
| 6) | + | | | | | | | | | + | | | | | | | | | + | | | | | | | | + | | | | | | | | | | + | Five episodes, as the interval between the sample is >7d in each case. |
| 7) | - | | | | | | | | | - | | | | | | | | | - | | | | | | | | - | | | | | | | | | | - | See example 6 |