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Diagnostika

VZV Serology and VZV Serum-CSF Diagnosis from medac

Competence - Quality - Continuity

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Gesellschaft für klinische Spezialpräparate mbH • GE Diagnostika • Theaterstrasse 6 • D-22880 Wedel
Phone ++49/4103/8006-0 • Fax ++49/4103/8006-359 • www.medac.de

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Importance

The varicella-zoster virus (VZV) is a member of the Herpesviridae family. It consists of a double-stranded DNA genome, nucleocapsid, tegument and virus envelope. Primary infections (varicella, chickenpox) generally occur in childhood. In most cases the symptoms of primary infection in immunocompetent patients are moderate. In immunosuppressed individuals VZV infection may lead to serious complications, such as CNS symptoms, pneumonia and secondary bacterial infections.

Serological prevalence in adults is approximately 95%. Following primary infection, the varicella-zoster virus typically persists for life in the sensory dorsal root ganglia and causes latent infection of neuronal cells. Endogenous reactivation of the virus may therefore result in the appearance of a secondary clinical condition called herpes zoster (shingles).

Disease associations

➤ Varicella (chickenpox)

Complications:
- Perinatal varicella infection of the newborn
- Congenital varicella infection
- Varicella meningitis
- Varicella pneumonia

➤ Zoster (shingles)

Complications:
- Generalised zoster in immunosuppressed individuals
- Post-herpetic neuralgia
- Encephalitis, encephalomyelitis
- Ramsay Hunt syndrome with facial nerve palsy

Antibody diagnosis

The diagnosis of varicella and zoster is made primarily on the basis of the typical clinical picture. However, specific laboratory diagnosis - taking account of VZV serology - is required in atypical disease patterns, as found in patients with immunodeficiency, infections during pregnancy and CNS disease and pneumonia.

While the detected presence of VZV-IgM and VZV-IgG is indicative of primary infection, reactivations are commonly characterised by VZV-IgA and a marked increase in VZV-IgG.

The goals of VZV antibody determination in immunocompetent patients are:

- To establish immune status
- To verify the success of immunisation
- To confirm a suspected diagnosis of varicella or zoster
- To identify infections with CNS involvement (serum-CSF diagnosis)

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Prophylaxis

Varicella (chickenpox) infections can be prevented by immunisation. In Germany the Standing Committee on Immunisation (STIKO) recommends varicella immunisation for all children, ideally between the ages of 11 and 14 months, and for adolescents without a history of varicella. In addition, active immunisation is recommended for defined risk groups (including seronegative women planning to have children, and seronegative patients prior to organ transplantation or immunosuppressive therapy). The vaccines currently on the market are highly efficient in terms of preventing primary VZV infection.

Advantages of medac assays

- VZV-IgG ELISA PKS medac is an assay system for the quantitative determination of specific IgG antibodies.
- By using assay controls that have been calibrated against the WHO international reference standard, it is possible to measure the specific anti-VZV-IgG level in mIU/ml.
- VZV-IgA ELISA PKS medac is an assay system for the quantitative determination of specific IgA antibodies (mAU/ml).
- Interference with high IgG titres and rheumatoid factors is avoided by subjecting all samples to IgG/RF absorption prior to IgA assay.
- VZV-IgG ELISA PKS medac and VZV-IgA ELISA PKS medac implement the principle of single-point quantification.
- VZV-IgG ELISA PKS medac and VZV-IgA ELISA PKS medac have been evaluated for serum-CSF diagnosis. The assays permit the detection of VZV-specific intrathecal antibody synthesis by determining a pathogen-specific antibody index in paired serum-CSF samples.
- VZV-IgM ELA Test PKS medac is based on the µ-capture principle and operates with an enzyme-labelled antigen. This assay design guarantees highly specific and sensitive IgM detection.
- The assays have been CE-certified in accordance with European Directive 98/79 on in-vitro diagnostic (IVD) medical devices.

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Sensitivity and specificity

The sensitivity and specificity of the medac assays have been determined by comparison with results obtained in samples with predefined status during routine diagnostic practice and are presented in the following 3 x 3 contingency tables:

VZV-IgG

Predefined status (n=150)

		Negative	Borderline	Positive
medac	Negative	49	0	0
	Borderline	0	1	0
	Positive	1	0	99

Sensitivity: 100% Concordance: 99,3%
Specificity: 98,0%

VZV-IgM

Predefined status (n=150)

		Negative	Borderline	Positive
medac	Negative	99	0	4
	Borderline	0	0	1
	Positive	1*	0	45

* Sample from a patient with confirmed recent VZV infection

Sensitivity: 90,0% Concordance: 96,0%
Specificity: 99,0%

VZV-IgA

Predefined status (n=161)

		Negative	Borderline	Positive
medac	Negative	54	1	2
	Borderline	1	0	0
	Positive	0	0	103

Sensitivity: 98,1% Concordance: 97,5%
Specificity: 98,2%

➤ **The medac assays permit highly specific and sensitive VZV antibody determination and, when performed in combination, they guarantee a reliable interpretation of VZV serological status.**

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Antigen

- Highly purified varicella-zoster virus preparation
- **E**nzyme **L**abelled **A**ntigen (ELA) for IgM detection, conjugated with horseradish peroxidase

Clinical features

- Possibility to discriminate between primary infection, reactivation and past infection
- Determination of immune status
- High sensitivity and specificity
- **IgM-ELA:** No unspecific reactions, no false positive results caused by rheumatoid factor due to ELA technique and µ-capture method
- No blocking of IgM antibodies by high IgG titers
- **IgG- and IgA-ELISA:** Also approved for detection of IgG and IgA antibodies in paired serum / cerebrospinal fluid (CSF)
- Suitable for parallel determination of immune status and pathogen-specific antibody index
- **IgA-ELISA:** IgG/Rf-absorbant eliminates blocking of IgA antibodies by high IgG titers

Technical features

- Pipetting Control System (PKS) with coloured reagents
- Breakable wells
- Rapid, automatable, use for large/small routine diagnosis
- Single-point quantification by a single calibrator (no calibration curve necessary)
- No additional calibration curve necessary for diagnosis in CSF
- Objective, reproducible, standardized results
- **IgG-ELISA:** Calibrated against the **WHO** reference preparation

Products

Test Kit	Cat.-No.	Determinations
VZV-IgM-ELA Test PKS medac	101-PKS	96x1
VZV-IgA-ELISA PKS medac	102-PKS	96x1
VZV-IgG-ELISA PKS medac	103-PKS	96x1

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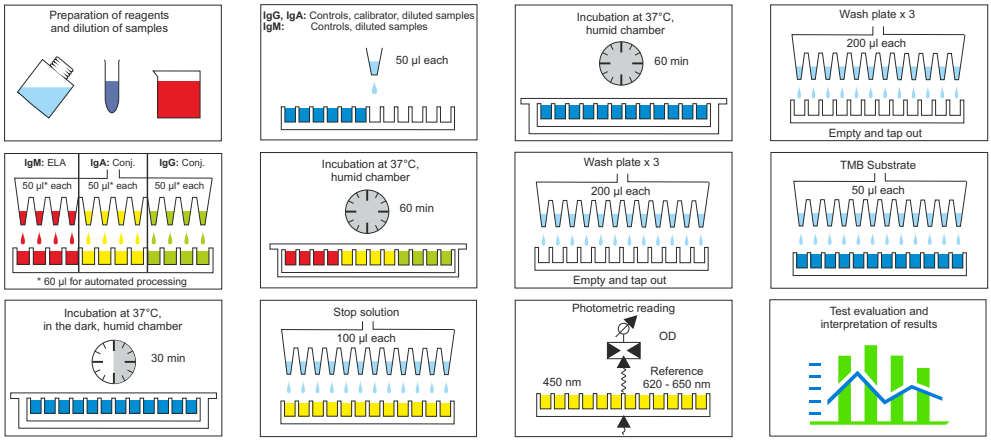
Test run



Calculation of results

- Subtract the OD value of the blank from all other OD values

VZV-IgG VZV-IgA

- The OD value of the negative control has to be < 0.150
- The lot-specific data sheet provided with the kit contains the following information:
  - Lot-specific calibration curve
  - Curve parameters a and b
  - Nominal OD value of the calibrator
  - Lower OD limit of the calibrator
  - Nominal concentration range of the positive control
- Calculation formula: Concentration = $b / \left(\frac{a}{OD_{corrected}} - 1 \right)$

VZV-IgG	Cut-off = 180 mIU/ml Grey zone = 160 - 200 mIU/ml
VZV-IgA	Cut-off = 250 mAU/ml Grey zone = 225 - 275 mAU/ml

VZV-IgM

- The mean OD value of the negative control has to be < 0.150
- The mean OD value of the positive control has to be > 0.600
- Cut-off = mean OD value of the negative control + 0.140
- Grey zone = Cut-off ±10%

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- Calculation of the mIU values as defined in VZV-IgG
- Calculation of the mAU values as defined in VZV-IgA
- Calculation of the pathogen-specific IgG and IgA quotient (Q_{spec}):

$$Q_{spec} = \frac{\text{Calculated quantity of spec. antibody liquor x dilution liquor}}{\text{Calculated quantity of spec. antibody serum x dilution serum}}$$

- Calculation of the antibody index (AI):

1. $AI = Q_{spec} / Q_{tot}$ (for $Q_{tot} < Q_{lim}$)
2. $AI = Q_{spec} / Q_{lim}$ (for $Q_{tot} > Q_{lim}$)
3. $Q_{lim} = 0{,}93 \times \sqrt{Q_{alb}^{\,2} + 6 \times 10^{-6}} - 1{,}7 \times 10^{-3}$ (for IgG)

   $Q_{lim} = 0{,}77 \times \sqrt{Q_{alb}^{\,2} + 23 \times 10^{-6}} - 3{,}1 \times 10^{-3}$ (for IgA)

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Contact:

Export Department:

medac GmbH
Diagnostic Division
Cornelia Appelius
Dr. Sabine Dettlaff
Dr. Karen Dreesbach
Theaterstrasse 6
D-22880 Wedel
phone.: ++49 4103 8006- 0
fax: ++49 4103 8006 -359
e-mail: c.appelius@medac.de
s.dettlaff@medac.de
k.dreesbach@medac.de

homepage: www.medac.de

Austria and Slovenia:

medac
Dr. Maria Kleindel
Postfach 20
A-3032 Eichgraben
mobile: ++43 676 502 25 69
fax: ++43 2773 43 574
e-mail: m.kleindel@medac.de

Belgium and Luxembourg:

medac
Georges Wauthier
8, rue des Bailleries
B-5081 Meux
phone: ++32 81 74 84 83
fax: ++32 81 74 84 83
e-mail: g.wauthier@medac.de

Czech Republic and Slovakia:

medac
Dr. Anna Manthey
P.O. Box 113
CZ-140 21 Prague 4
phone: ++42 02 41 40 26 18
fax: ++42 02 41 40 26 18
e-mail: a.manthey@medac.de

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