EUROIMMUN Medizinische Labordiagnostika AG

Bordetella pertussis infections

Professional diagnostics of whooping cough

- **Guideline-compliant ELISA test systems for the detection of whooping cough**
- **Species-specific antibody determination and quantification in international units by means of Anti-Bordetella pertussis Toxin ELISA (IgA, IgG)**
- **Efficient automation solutions**

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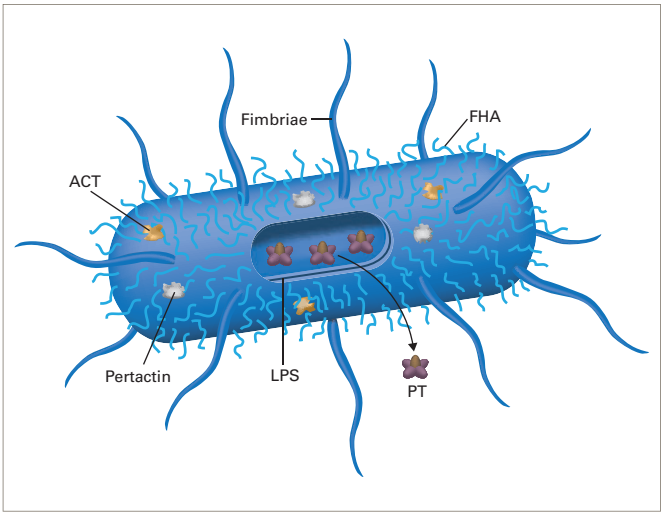
Bordetella pertussis

Bordetella are gram-negative coccobacilli coated by a capsule with diverse virulence factors. Five out of nine known *Bordetella* species cause respiratory diseases in humans. *B. pertussis* and B. parapertussis have particular clinical relevance. Transmission between humans takes place via aerosols and smear infections. Following a *B. pertussis* infection, the first symptoms appear after an incubation period of approximately 7–14 days. The disease is usually divided into 3 stages:

- Catarrhal stage: Flu-like symptoms with moderate fever; approx. 1–2 weeks.
- Convulsive stage: Staccato-like cough, especially at night, often with vomiting of mucus, followed by inspiratory whoops, approx. 4–6 weeks.
- Decremental stage: Abating of the cough within 6–10 weeks.



Bordetella pertussis

The typical symptoms of whooping cough are mainly observed in children. In adolescents and adults, however, the disease manifests as ongoing cough without the typical coughing fits. In unvaccinated babies, whooping cough usually progresses atypically with apnoea. Moreover, severe complications such as secondary pneumonia or otitis may occur. Infection or vaccination lead to specific immunity which is limited to some years.

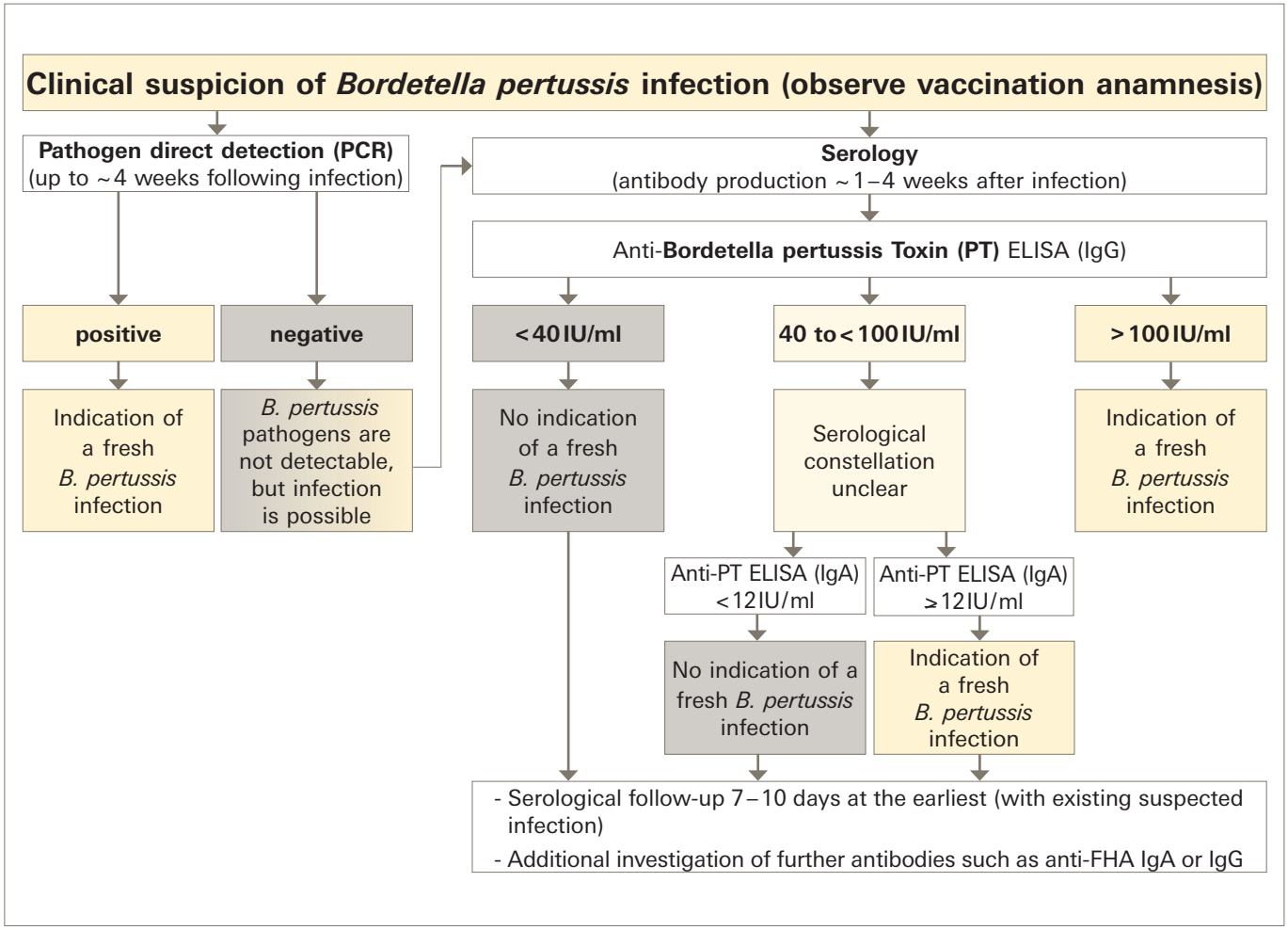
The clinical progression of an infection depends on the formation of different toxins and adhesins. These encompass especially pertussis toxin (PT) and filamentous haemagglutinin (FHA), as well as adenylate cyclase toxin (ACT), pertactin and lipopolysaccharides (LPS). The combination of these factors protects the bacterium from the host's immune system and helps its spread in the airways. PT is exclusively produced by *B. pertussis* and is therefore especially relevant as a highly specific antigen in serological diagnostics.

Antigen	Relevance
Pertussis toxin (PT)	■ Species-specific of *B. pertussis* ■ Exclusion of B. parapertussis infections ■ Component of acellular vaccines, so that anti-PT antibodies are detectable both after an infection and vaccination
Filamentous haemagglutinin (FHA)	■ Bordetella-specific (all species) ■ Component of acellular vaccines, so that anti-FHA antibodies are detectable both after an infection and vaccination

Diagnostics

At early stages of the disease, the direct pathogen detection by means of culture or PCR from nasopharyngeal smears is useful for the diagnosis of a *Bordetella* infection. From the convulsive stage on, serology plays an important role since the pathogen is then no longer detectable in the respiratory tract. Here, the following recommendations and indications apply[1-4]:

- Antibody determination in international units IU/ml according to WHO standards (see Diagnostic scheme)
- Use of ELISA test systems for the determination of specific antibodies against PT; quantification of the antibody titer, exclusion of *B. parapertussis* infections.
- If applicable, determination of IgA titer against PT; this has a lower diagnostic value than IgG determination.
- The IgM response provides less information for the diagnosis since it is mostly directed against unspecific antigens such as LPS and fimbriae.
- Measurable antibody concentrations do not provide information on existing protection or the duration of immunity following vaccination.

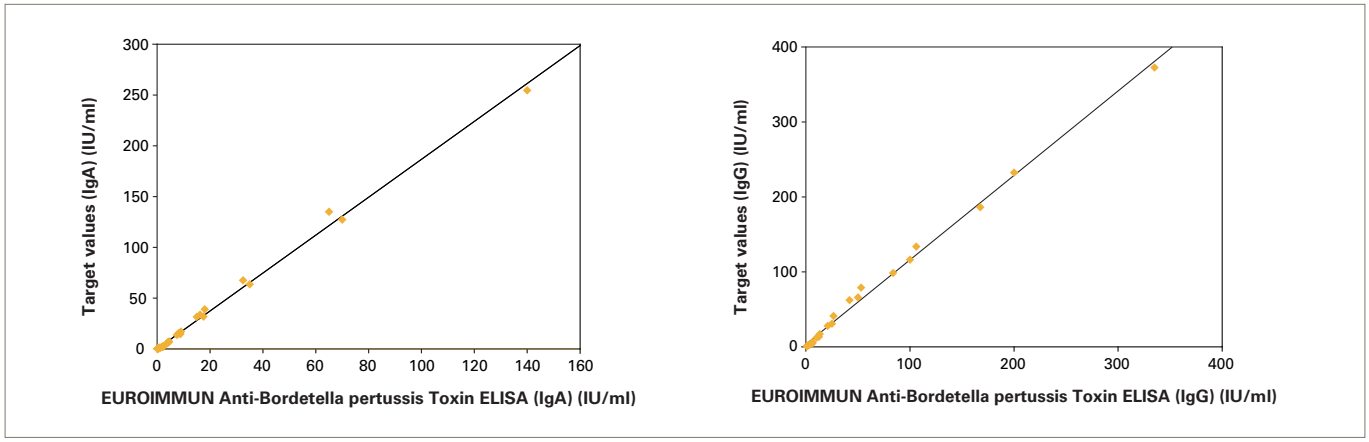


Adapted according to Riffelmann et al., 2010

EUROIMMUN Anti-Bordetella pertussis Toxin ELISA (IgA, IgG)

- Corresponds to the recommendations by international reference institutes [1-4]
- Species-specific antibody detection for *B. pertussis*; no cross reactions through antibodies against *B. parapertussis* or other bacteria
- Based on native, highly purified pertussis toxin
- Quantification in IU/ml based on the first international standard of the WHO
- Fully automatable, e.g. with EUROIMMUN Analyzer I and EUROLabWorkstation ELISA

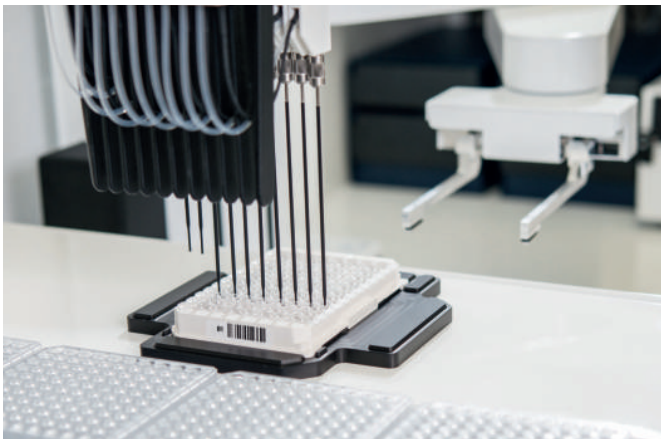
In 4 or 3 reference sera* anti-*Bordetella pertussis* toxin antibodies (IgA or IgG), were investigated in different concentrations with the EUROIMMUN Anti-Bordetella pertussis Toxin ELISA (IgA or IgG). The linear regression analysis yielded a regression coefficient of $r^2 = 0.99$.



* 1st serum: WHO international standard (lot 06/140); 2nd serum: WHO reference serum (lot 06/142); 3rd serum: FDA US reference serum lots 3&4; 4th serum: FDA US reference serum lot 5

77 and 73 clinically characterised patient samples (INSTAND quality assessment, Germany; Labquality, Finland) were tested using the EUROIMMUN Anti-Bordetella pertussis Toxin ELISA (IgA or IgG). The sensitivity amounted to 97% for the IgA and 98% for the IgG test. The specificity amounted to 100% for both (borderline sera excluded).

EUROIMMUN Anti-B. Pertussis Toxin ELISA		INSTAND/Labquality		
		positive	borderline	negative
IgA (n = 77)	positive	37	0	0
	borderline	0	1	0
	negative	1	0	38
IgG (n = 73)	positive	45	0	0
	borderline	0	0	0
	negative	1	3	24



Ordering

Test systems for *Bordetella* diagnostics	Order number
Anti-Bordetella pertussis Toxin ELISA (IgA, IgG)	EI 2050-9601 A, G
Anti-Bordetella FHA ELISA (IgA, IgG)	EI 2050-9601-3 A, G
EUROLINE Anti-Bordetella pertussis (IgA, IgG)	DN 2050-#### A, G

Literature

1. Podbielski M, et al. (Hrsg.). **MiQ 35a. Infektionsimmunologische Methoden Teil I (2016).**
2. Guiso N, et al. **What to do and what not to do in serological diagnosis of pertussis: recommendations from EU reference laboratories.** Eur J Clin Microbiol Infect Dis 30(3):307–312 (2011).
3. Cherry JD, et al. **Clinical definitions of pertussis: summary of a Global Pertussis Initiative roundtable meeting, February 2011.** Clin Infect Dis 54(12):1756–1764 (2012).
4. Riffelmann M, et al. **Performance of commercial enzyme-linked immunosorbent assays for detection of antibodies to Bordetella pertussis.** J Clin Microbiol 48(12):4459–4463 (2010).