Catlab Informa

Bulletin N. 143

WHOOPING COUGH IS ON THE RISE: EPIDEMIOLOGICAL SITUATION IN THE VALLÈS AREA.

Pertussis or whooping cough is an endemic disease caused by the bacteria *Bordetella pertussis* and specifically by the pertussis *toxin that* can affect people of all ages. Its outbreaks are characterized because maintain a pattern epidemic cyclical with waves occuring every 3-5 years. Pertussis is a notificable disease that since late 2023 has re- emerged in Catalonia and worldwid.

In addition to *B. pertussis*, three other *Bordetella* species can cause disease: *B. parapertussis*, *B. holmesii*, and *B. bronchiseptica*. The disease caused by *B. parapertussis* is similar to whooping cough, but further mild, since *B. parapertussis does* not produce *pertussis* toxin.

PATHOGENY

B. pertussis is transmitted by direct contact or inhalation of small respiratory droplets expelled by infected persons when coughing. The bacteria adhere to the ciliated epithelium of the upper respiratory tract. They multiply and express several virulence factors that promote colonization and evasion of the host complement system[1]. (Figure 1)

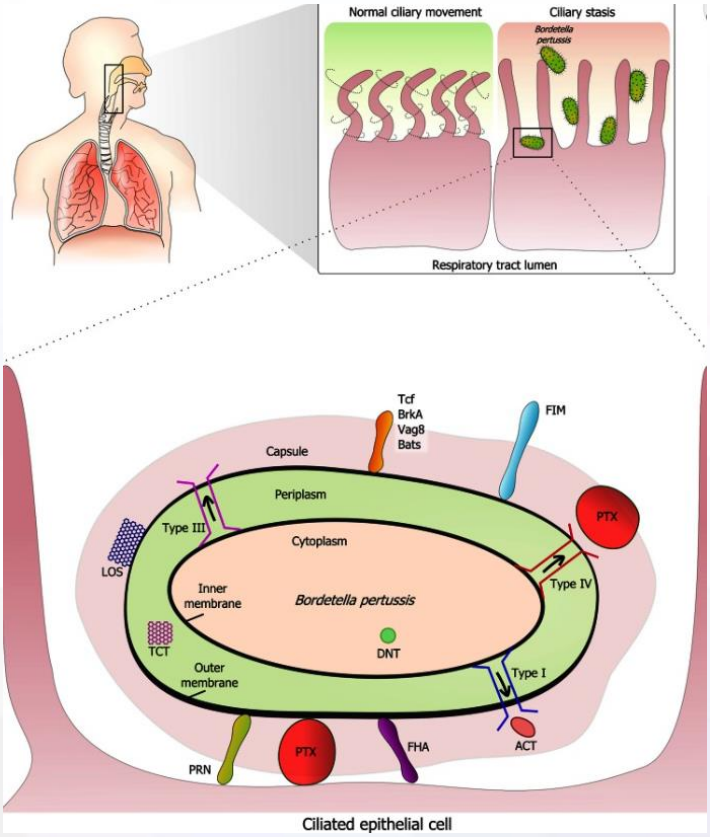


Figure 1: Adhesion and entry into the epithelial cell of B. pertussis

B. pertussis interacts with the ciliated epithelium of the trachea, bronchi and bronchioles. Several *B. pertussis proteins* are involved in adherence to host receptors, including:

a) Toxins, endotoxins and secretion systems:
- Pertussis toxin (Ptx)
- Cytotoxin (TCT)
- Lipopolysaccharide (LOS)
- Dermonecrotic toxin (DNT)
- Type III secretion system

b) Adhesins and other factors involved in adhesion:
- Pertactin (Prn)
- Hemagglutinin (FHA)
- Fimbriae (FIM)
- Tracheal colonization factor A (TcfA)
- Carrier Protein C

c) Serum resistance factors:
- *Bordetella* resistance to the destroyer protein A (BrkA)
- Auto transporter (Vag8)

Some of these proteins will be part of the vaccine we use today to combat this disease.

SYMPTOMS:

Pertussis has an incubation period of 7 to 10 days, but can last up to 21 days. After this incubation period, the disease begins and is characterized by three classic phases [2]:

1. **Catarrhal phase:** symptoms similar to those of a common cold (rhinitis, sneezing, non-purulent conjunctivitis, low-grade fever and mild intermittent non-productive cough) that gradually becomes more intense. This phase usually lasts 1 to 2 weeks and is highly contagious.

2. **Paroxysmal phase**: dry cough that increases in the form of severe coughing attacks, which may get worse during the night. Paroxysmal cough usually ends with a long inspiratory effort accompanied by 'inspiratory whoop' sound at the end. Vomiting after coughing, nausea, shortness of breath, exhaustion and sweating may occur.

   There may be a low-grade fever or nothing at all. Children, especially those younger than 6 months, may have apnea instead of stridor. This phase lasts 3 to 6 weeks.

3. **Convalescence phase** duration of 1 to 12 weeks, coughing attacks gradually disappear.

CLINICAL COMPLICATIONS:

Clinical complications of Pertussis in the pediatric population have decreased thanks to systematic vaccination in both children and pregnant women. Although it is true that the most serious complications occur in children, children under six months of age, premature newborns and unvaccinated infants are part of the most vulnerable group in this situation.

In children under 3 months of age, it may present as severe whooping cough, " **malignant whooping cough**," and may be accompanied by complications, characterized by rapid progression to respiratory failure, cyanosis, severe leukocytosis and lymphocytosis, neurological manifestations, sepsis, pneumonia, and pulmonary hypertension, which may leave significant sequelae and even cause the death of the patient.

MICROBIOLOGICAL DIAGNOSIS:

There are two types of approach to the diagnosis of whooping cough:

- **Indirect diagnosis**: serological tests that detect antibodies against pertussis toxin (anti-pertussis toxin, anti-PTX).

- **Direct diagnosis**: isolation of *B. pertussis* by culture (gold standard) *and* specific nucleic acid amplification tests.

Direct diagnostic methods, and in particular the PCR test, are the preferred option for diagnosis in the acute phase, with greater specificity than indirect diagnostic methods. The latter are reserved for situations where at least two to four weeks have passed since the onset of the cough. Even so, since elevated levels of IgG can be detected for more than a year after natural infection or vaccination, the use of serology may lead to the detection of false positives. (Figure 2) [3]

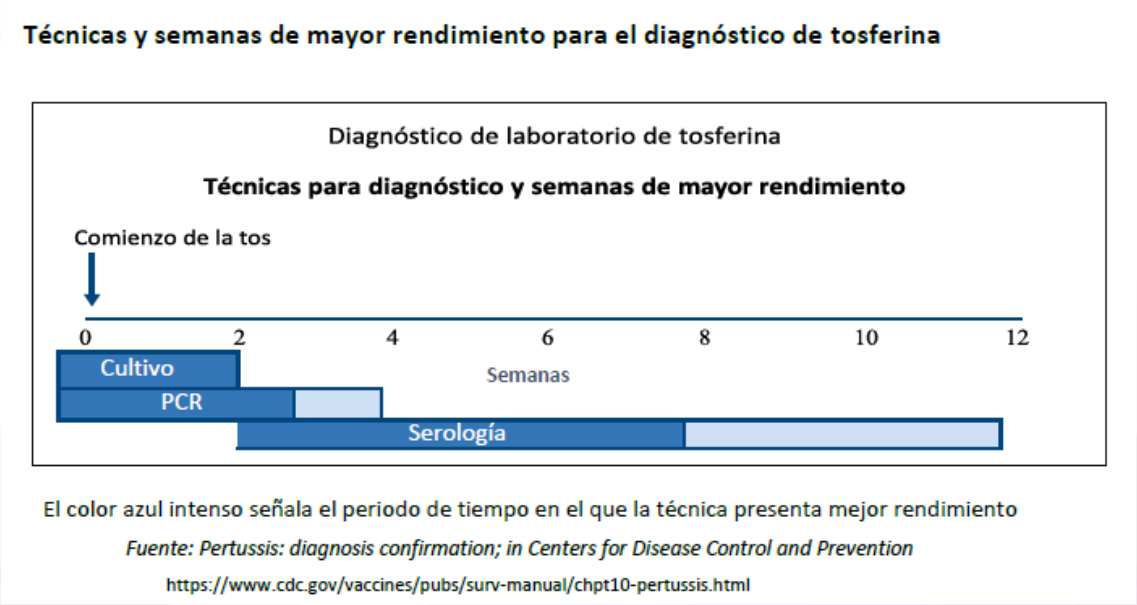


Figure 2: Pertussis Laboratory Diagnosis

The ideal sample for molecular detection is a nasopharyngeal aspirate or nasopharyngeal swab collected in a swab with liquid medium (never cotton or calcium alginate).

Molecular detection of *B. pertussis* (IS481, ptxA targets) in the CATLAB Laboratory is carried out by multiple qualitative real-time PCR using the Bordetella reagent Elite MGB®Kit (ELITechGroup) and the Elite Ingenius® equipment. This PCR also detects *B. parapertussis* (IS1001 target) and *B. holmessi* (IS481 and recA targets). (Figure 3)

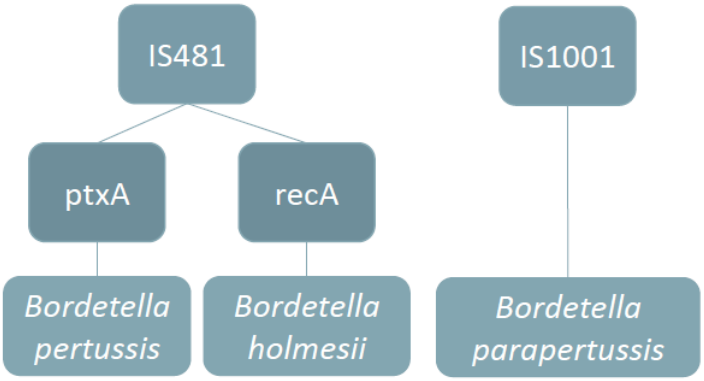


Figure 3: Molecular detection targets using real-time PCR

TREATMENT:

The treatment of choice is azithromycin (macrolide), administered on a 3-day regimen, except for children under 6 months of age, where it is administered on a 5-day regimen. The earlier treatment is started, the shorter the duration of infection and the lower the risk of transmission.[4]

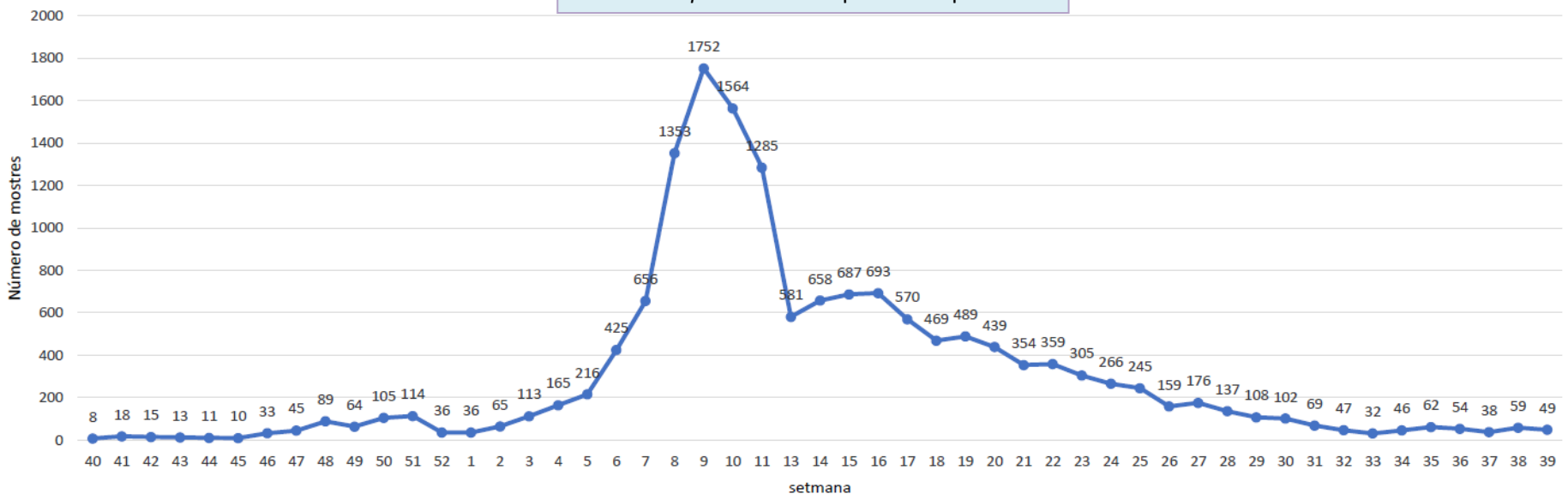
MICROBIOLOGY LABORATORY DATA

A total of 16,204 nasopharyngeal swab and aspirate samples have been processed using real-time PCR since the end of 2023.

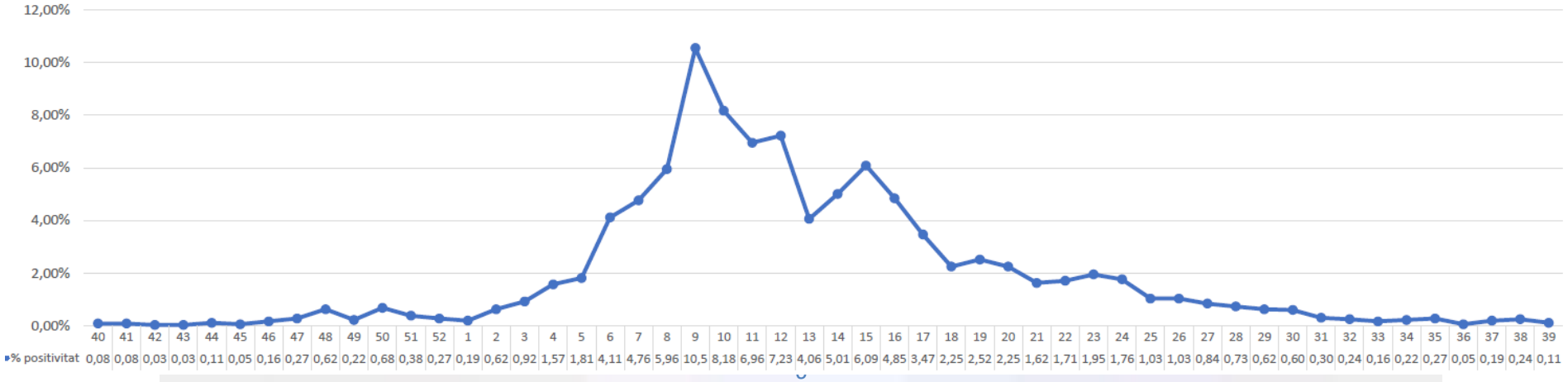
The data on the number of samples processed per week and the percentage of positivity are shown in the graphs below. (Graph 1 and 2)

Catlab Informa

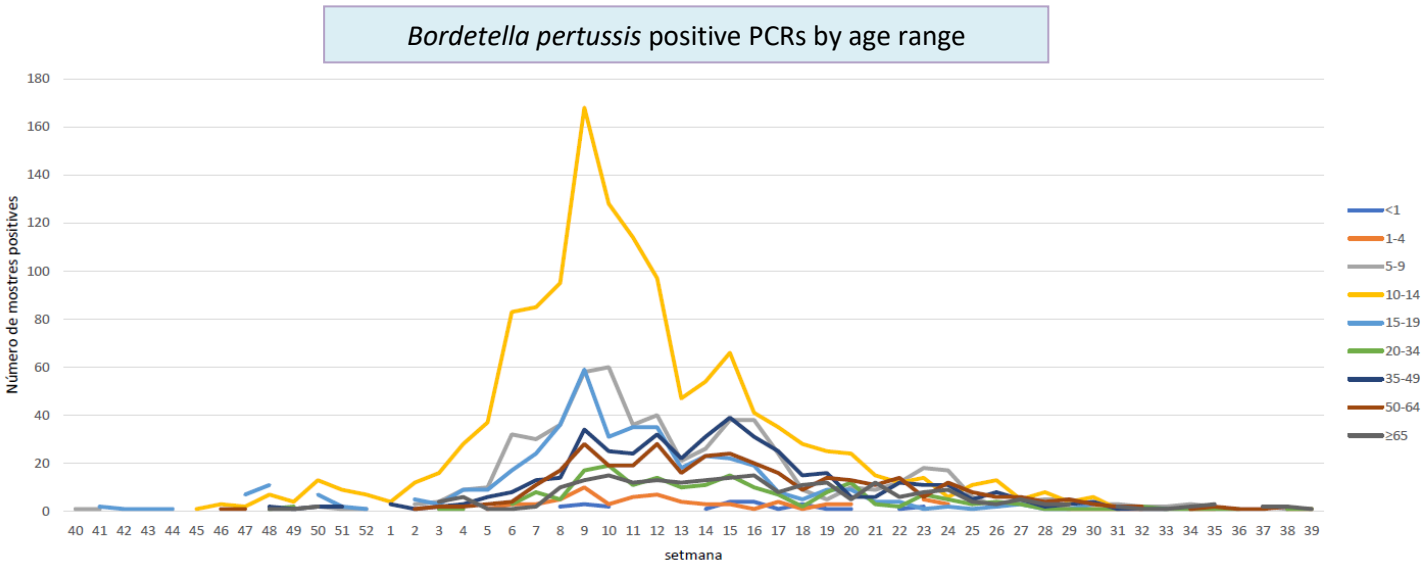
Bordetella pertussis PCRs processed per week



% Bordetella pertussis PCR positivity per week



Regarding the distribution of *Bordetella pertussis* positive PCRs by age, a peak was observed in the 10-14 years age range throughout the outbreak.



Up to April 2024 there were a total of 22 positive PCRs for *Bordetella pertussis* in patients under 1 year of age. Of these, 8 (36%) required hospital admission, 5 of them required ICU admission (62%), 3 were younger than 2 months of age and two were over 2 months of age. The 5 admitted to the ICU were not vaccinated with the DTaP vaccine. (Figure 4) [5]

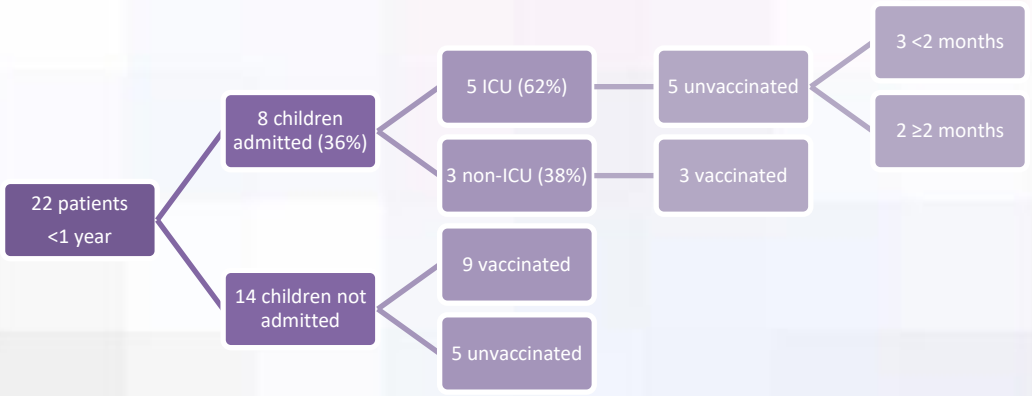


Figure 4: Patients under 1 year of age with positive PCR for Bordetella pertussis

It should be noted that children not currently vaccinated with the DTaP (Diphtheria-Tetanus-Pertussis Vaccine) are also not vaccinated against Poliomyelitis, *Haemophilus influenzae* b, Hepatitis B virus, tetanus and diphtheria.

REFERENCES:

1. Jongerius I, Schuijt TJ, Mooi FR, Pinelli E. Complement evasion by Bordetella pertussis: implications for improving current vaccines. J Mol Med (Berl). 2015 Apr;93(4):395-402. doi: 10.1007/s00109-015-1259-1. Epub 2015 Feb 18. PMID: 25686752; PMCID: PMC4366546.

2. Protocol per a la vigilància i el control de la tos ferina a Catalunya Agència de Salut Pública de Catalunya 30 d'abril de 2024 Disponible a https://scientiasalut gencat cat/bitstream/handle/ 11351 11316 /protocol_vigilancia_control_tos_ferina_ 2024 pdf? sequence= 6 &isAllowed=y [consultar septiembre 2024]

3. Protocolo de vigilancia de tosferina. Actualización de julio del 2024. Disponible a https;// cne.isciii.es/documents/d/cne/protocolo-de-vigilancia-de-tosferina

4. Ivaska L, Barkoff AM, Mertsola J, He Q. Macrolide Resistance in Bordetella pertussis: Current Situation and Future Challenges. Antibiotics Basel). 2022 Nov 7;11(11):1570. DOI: 10.3390/antibiotics11111570. PMID: 36358225

5. Documents de Vigilància Epidemiològica. Vallès Occidental i Vallès Oriental. Epidemiologia de la tos ferina al 2024 al Vallès. Abril 2024.

Mireia Rajadell Guiu
Microbiology Department
CATLAB
Tel. 93.748.56.00 - ext. 35002 / 620372209
mrajadell@catlab.cat

Genoveva Santillana Cernuda
Microbiology Department
CATLAB
Tel. 93.748.56.00 - ext. 35002 / 683195255
gsantillana@catlab.cat