Bordetella pertussis
Epidemiology and diagnostic tools in Belgium

Denis Piérard

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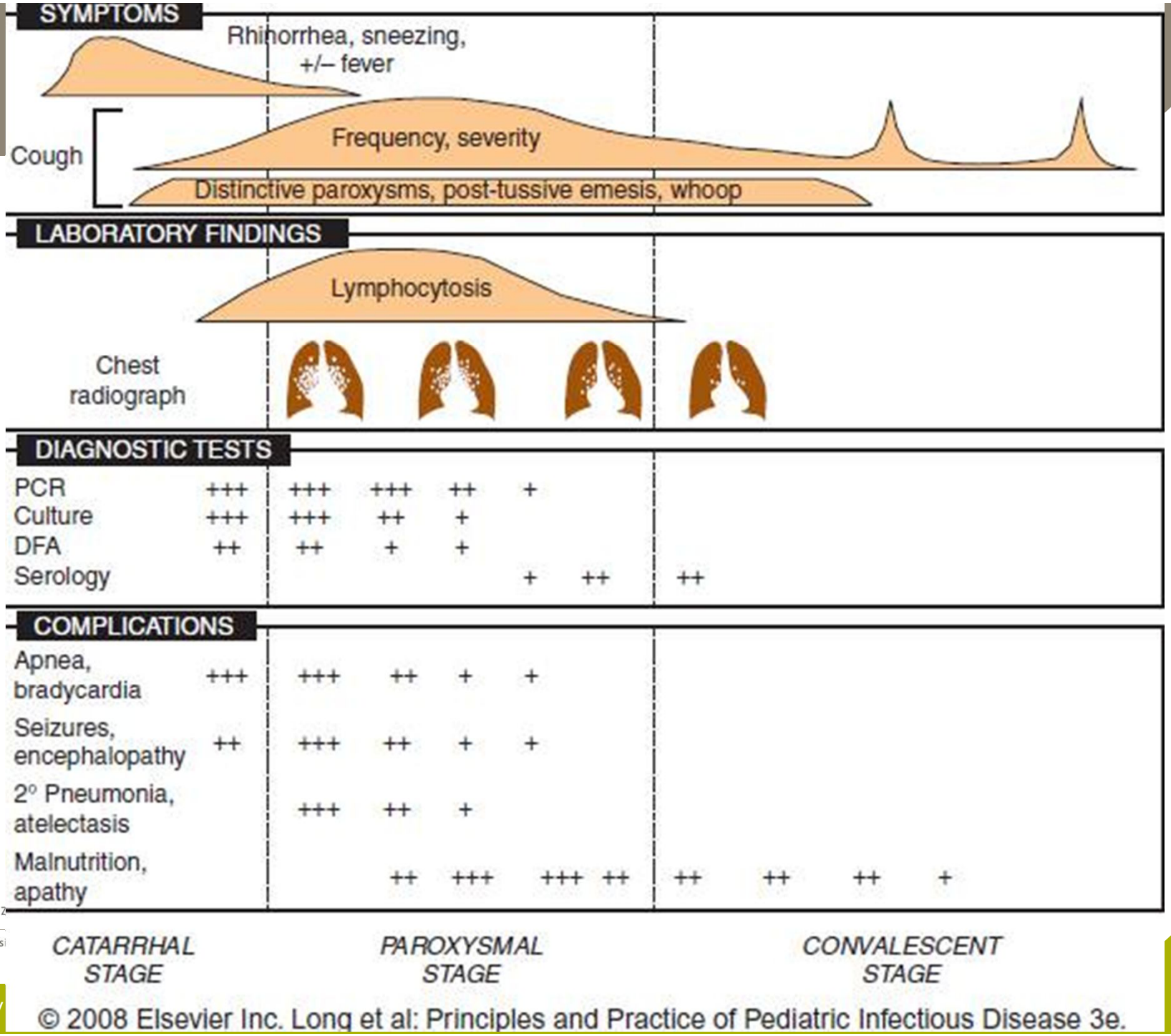
SYMPTOMS
Rhinorrhea, sneezing, +/– fever
Cough
Frequency, severity
Distinctive paroxysms, post-tussive emesis, whoop
LABORATORY FINDINGS
Lymphocytosis
Chest radiograph
DIAGNOSTIC TESTS
PCR +++ +++ +++ ++ +
Culture +++ +++ ++ +
DFA ++ ++ + +
Serology + ++ ++
COMPLICATIONS
Apnea, bradycardia +++ +++ ++ + +
Seizures, encephalopathy ++ +++ ++ + +
2° Pneumonia, atelectasis +++ ++ +
Malnutrition, apathy ++ +++ +++ ++ ++ ++ ++ +
CATARRHAL STAGE
PAROXYSMAL STAGE
CONVALESCENT STAGE
© 2008 Elsevier Inc. Long et al: Principles and Practice of Pediatric Infectious Disease 3e.

Clinical manifestations

- Classical pertussis (mainly in unimmunized toddlers and children)
  - → 3 stages, after incubation of 7 to 10 days (range 5 to 21 days)
    - Catarrhal: nondistinctive catarrhal symptoms
    - Paroxysms of cough with inspiring whoop and often post-tussive vomiting
    - Convalescent phase: , with recurrence of paroxysmal cough for up to 1 year
- Atypical pertussis
  - → Infants: less inspiratory whoop but gagging, gasping, cyanosis, apnea and prolonged convalescent phase
  - → Immunized children and adults: all stages foreshortened, often without paroxysms and without distinct stages

Clinical manifestations, atypical disease in babies
Severe and unrecognised: pertussis in UK infants

- Crowcroft et al. Arch Dis Child 2003; 88: 802-806

  Inclusion:
  - → n=142 infants < 5 m, admission in PICU
  - → resp failure – ALTE
  - → systematically specimen collection for microbiology (incl *B pertussis*)

  Results:
  - → 23% (n=33) pertussis confirmed (PCR, culture)
    - 33% co-infection with RSV
    - n=2 cases of fatality
- Conclusion:
  - → severe pertussis is “atypical” and underdiagnosed
  - → clinical diagnosis is difficult
  - → RSV co-infection does not exclude pertussis and can aggravate clinical course

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Clinical manifestations, atypical disease in oldies

A Pertussis Outbreak Associated with Social Isolation among Elderly Nuns in a Convent

Mertens et al. Clin Infect Dis 2007; 44:266-8

- Outbreak in a Dutch convent in 1992, recognized at week 10; cohort study started at week 12. Total: 66 cases / 75 n
- Diagnosis: PCR, culture, significant change (3-fold) in IgG ab titres at weeks 9, 13 and 60 or single titre > 100 U/ml
- Incidence rates
  - → 75 retired nuns (none vaccinated) IR = 60%
    - 9 with life-long career in convent IR = 100%
    - 66 with career outside convent IR = 55% P = 0,007

      of which:

      only in Dutch society IR = 74%
      only in tropics IR = 35%
      both IR = 17% P < 0,0001
  - → 24 staff members (21 vaccinated) IR = 8%
- Mortality

  3/4 deaths were among nuns in age group 85-94 years

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Clinical manifestations, atypical disease in oldies

A Pertussis Outbreak Associated with Social Isolation among Elderly Nuns in a Convent

Table 1. Relationship between pertussis incidence, age, and duration of isolation from society among 75 nuns with (n = 66) and nuns without (n = 9) a career outside the convent.

Group	Pertussis incidence			Duration of cough among nuns with pertussis		No. of deaths among nuns with pertussis
	No. with pertussis/total	Percentage	P for linear trend in proportions	Median days (range)	P for trend on rank	
Age group, years			.31		.20	
55–64	8/16[a]	50		41[b] (28–98)		1
65–74	13/21	62		67 (14–268)		0
75–84	16/27	59		51 (11–178)		0
85–94	8/11[a]	73		83[b] (28–236)		3
Duration of isolation from society,[c] years			.005		.72	
0–6	5/15	33		55 (28–173)		1
7–13	9/17	53		38 (14–268)		0
14–20	10/16	63		88 (11–178)		1
21–34	9/12	75		45 (30–236)		1
35–70	12/15	80		53 (14–159)		1

[a] No significant difference between the incidence of pertussis in the youngest and oldest age group (P = .21, Fisher's exact test).
[b] No significant difference between the median duration of cough in the youngest and oldest age group (P = .10).
[c] Duration of isolation of the 9 nuns without a career outside the convent and the duration of isolation since retirement of the 66 nuns with a career outside the convent.

Discussion: waning immunity due to social isolation in women born in1898-1936, when 100% of population experienced pertussis before 15 years of age

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SHORT REPORT
Bordetella pertussis seroprevalence in Belgian adults aged 20–39 years, 2012

K. HUYGEN[1]*, C. RODEGHIERO[1], D. GOVAERTS[2], I. LEROUX-ROELS[3], P. MELIN[4], M. REYNDERS[5], S. VAN DER MEEREN[6], S. VAN DEN WIJNGAERT[7] AND D. PIERARD[6]

In the context of the Eupert-Labnet WP6 seroprevalence study (comparing sera from 14 European member states), 1500 **anonymized leftover** diagnostic samples were collected randomly during the second semester of 2012 by the laboratories of clinical biology of **six** participating **Belgian** centres, equally distributed between Flanders, Wallonia and Brussels Capital region. A total of 750 samples (125/ centre) were selected from subjects in the age group 20-29 years and 750 samples (125/ centre) from subjects in the age group 30-39 years.

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Conclusion of seroprevalence study

Sixty-one (4%) sera were indicative of an infection in the past two years (between 50 and 100 IU/ml) and another sixty-one (4%) sera had anti-PT IgG antibodies reflecting acute infection (> 100 IU/ml).

These results highlight the presence of a *Bordetella pertussis* reservoir in the adult 'healthy' Belgian population

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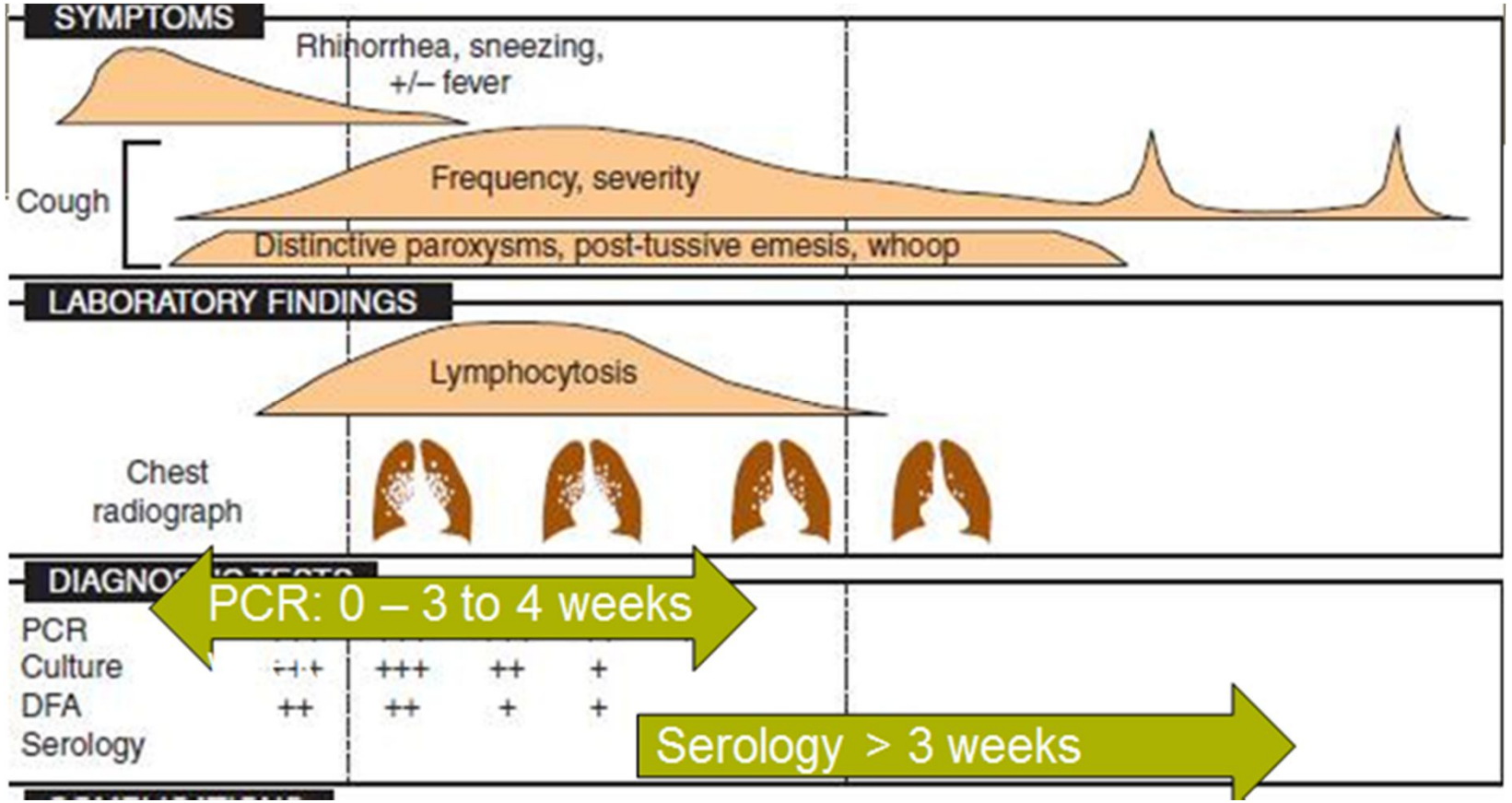
Laboratory diagnosis



Only Bordetella pertussis is included in the ECDC diagnosis of pertussis

- ***Bordetella pertussis***

  Exclusively isolated from humans, as agent of whooping cough *(has also been isolated from alveolar macrophages and blood)*

- ***Bordetella parapertussis***

  Pertussis-like disease (no pertussis for ECDC)

  (mild cases: 20% pertussis, 40% aspecific bronchitis, 40% asymptomatic)

  Also found in sheep

- ***Bordetella holmesii***

  Rare cause of respiratory or not respiratory infections in humans, recently isolated from patients with pertussis-like disease

- ***Bordetella bronchiseptica***

  Respiratory pathogen for and commensal of many animals, incl. dog, pig, cat & rabbit

  Humans: rare cases of pertussis-like disease, opportunistic in immuundeficient patients

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Vaccine-preventable diseases

- News
- Events
- Publications
- Surveillance reports
- Public health developments
- Scientific advances
- Eurosurveillance articles
- National plans

EU-IBD

EUVACnet

Case definitions

- Measles
- Mumps
- Rubella
- Pertussis
- Congenital rubella

Pertussis

Pertussis *(Bordetella pertussis)*

The case definition and classification is that stipulated by EU Commission Decision of 8 August 2012.

Clinical criteria:
Any person with a cough lasting at least two weeks and at least one of the following three:

- Paroxysms of coughing
- Inspiratory "whooping"
- Post-tussive vomiting

or

Any person diagnosed as pertussis by a physician

or

Apnoeic episodes in infants

Laboratory criteria:

At least one of the following three:

- Isolation of Bordetella pertussis from a clinical specimen
- Detection of Bordetella pertussis nucleic acid in a clinical specimen
- Bordetella pertussis specific antibody response

Serology results need to be interpreted according to the vaccination status

Epidemiological criteria:

Structure NRC

Two labs

→ UZ Brussel
- Diagnosis on respiratory samples (PCR; culture for strain typing)
- Most useful for young children
- Confirmation of diagnosis/strain identification for other labs

→ WIV-ISP
- Serological diagnosis (anti-PT IgG; not applicable if vaccine dosis < 1 year)
- Mostly samples from adults, generally one-point > 3 weeks symptoms

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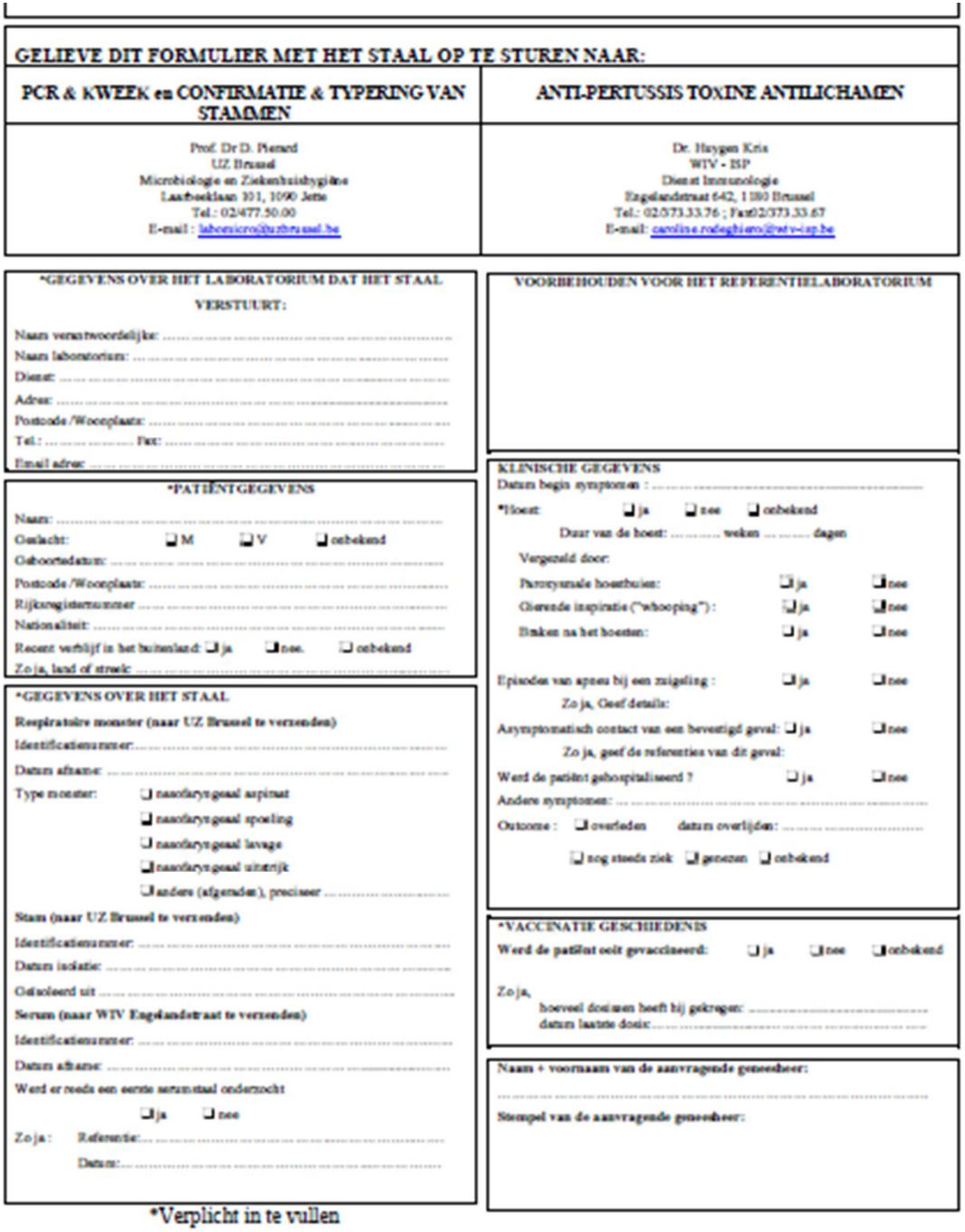

GELIEVE DIT FORMULIER MET HET STAAL OP TE STUREN NAAR:

PCR & KWEEK en CONFIRMATIE & TYPERING VAN STAMMEN	ANTI-PERTUSSIS TOXINE ANTILICHAMEN
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*GEGEVENS OVER HET LABORATORIUM DAT HET STAAL VERSTUURT:

Naam verantwoordelijke: .....
Naam laboratorium: .....
Dienst: .....
Adres: .....
Postcode /Woonplaats: .....
Tel.: ..... Fax: .....
Email adres: .....

VOORBEHOUDEN VOOR HET REFERENTIELABORATORIUM

*PATIËNTGEGEVENS

Naam: .....
Geslacht: ❑ M ❑ V ❑ onbekend
Geboortedatum: .....
Postcode /Woonplaats: .....
Rijksregisternummer .....
Nationaliteit: .....
Recent verblijf in het buitenland: ❑ ja ❑ neo. ❑ onbekend
Zo ja, land of streek: .....

KLINISCHE GEGEVENS

Datum begin symptomen : .....
*Hoest: ❑ ja ❑ nee ❑ onbekend
Duur van de hoest: ..... weken ..... dagen
Vergezeld door:
Paroxysmale hoesthuien: ❑ ja ❑ nee
Gierende inspiratie ("whooping"): ❑ ja ❑ nee
Braken na het hoesten: ❑ ja ❑ nee
Episodes van apneu bij een zuigeling : ❑ ja ❑ nee
Zo ja, Geef details:
Asymptomatisch contact van een bevestigd geval: ❑ ja ❑ nee
Zo ja, geef de referenties van dit geval:
Werd de patiënt gehospitaliseerd ? ❑ ja ❑ nee
Andere symptomen: .....
Outcome : ❑ overleden datum overlijden: .....
❑ nog steeds ziek ❑ genezen ❑ onbekend

*GEGEVENS OVER HET STAAL

Respiratoire monster (naar UZ Brussel te verzenden)
Identificatienummer: .....
Datum afname: .....
Type monster: ❑ nasofaryngeaal aspiraat
❑ nasofaryngeaal spoeling
❑ nasofaryngeaal lavage
❑ nasofaryngeaal uitstrijk
❑ andere (afgeraden), preciseer .....
Stam (naar UZ Brussel te verzenden)
Identificatienummer: .....
Datum isolatie: .....
Geïsoleerd uit .....
Serum (naar WIV Engelandstraat te verzenden)
Identificatienummer: .....
Datum afname: .....
Werd er reeds een eerste serumstaal onderzocht
❑ ja ❑ nee
Zo ja: Referentie: .....
Datum: .....

*VACCINATIE GESCHIEDENIS

Werd de patiënt ooit gevaccineerd: ❑ ja ❑ nee ❑ onbekend
Zo ja,
hoeveel dosissen heeft hij gekregen: .....
datum laatste dosis: .....

Naam + voornaam van de aanvragende geneesheer:
.....
Stempel van de aanvragende geneesheer:

*Verplicht in te vullen

NRC pertussis

Most important data

- Duration of symptoms
- Vaccination

Real-time PCR: which target for which species?

- Screening assay: IS481-IS1001
  - → High sensitivity: high copy number
  - → Low specificity
- Confirmation assay: IS1002-recA
  - → Lower sensitivity
  - → Specificity is high in combination with first assay
- At first other assays were only performed after positive result in screening
  - → practical difficulties
  - → performing both at the same time

	B. pertussis	B. parapertussis	B. holmesii	B. bronchiseptica
IS481	+++	-	++	+/-
IS1001	-	++	-	+/-
IS1002	+	+	-	+/-
recA	-	-	+	-

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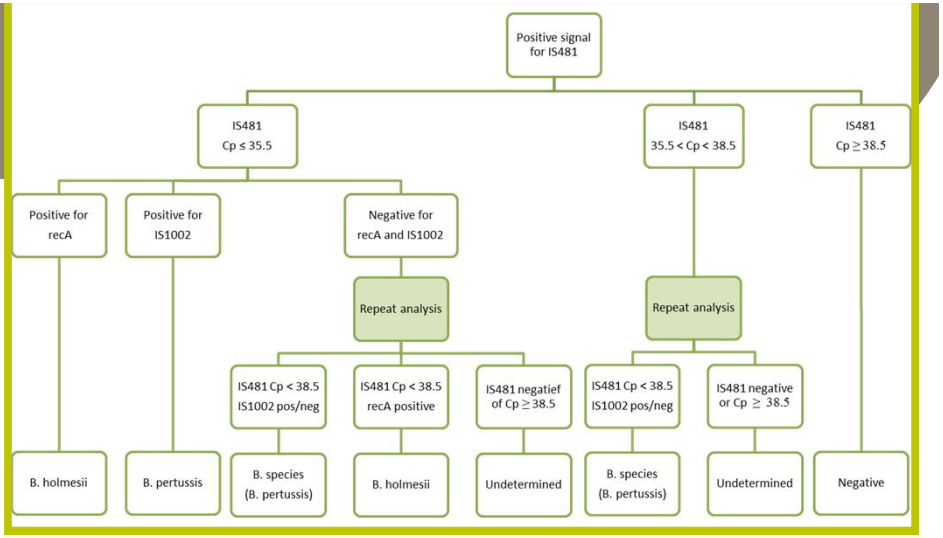
PCR interpretation

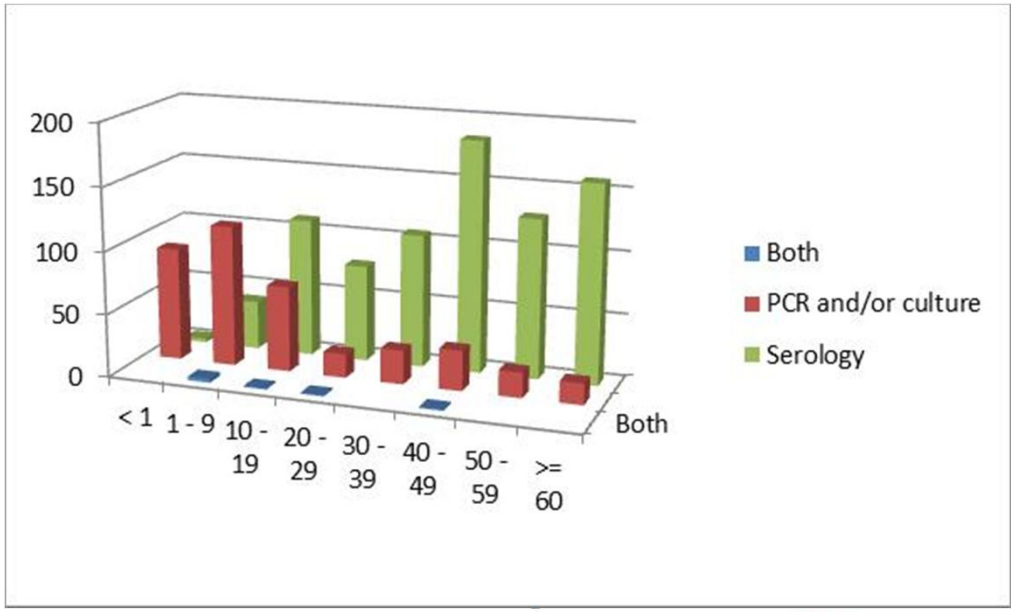
- Sensitivity
  - IS481: 3 CFU/PCR
  - IS1001: 5 CFU/PCR
  - recA: 52 CFU/PCR
  - IS1002: +/- 40 CFU/PCR

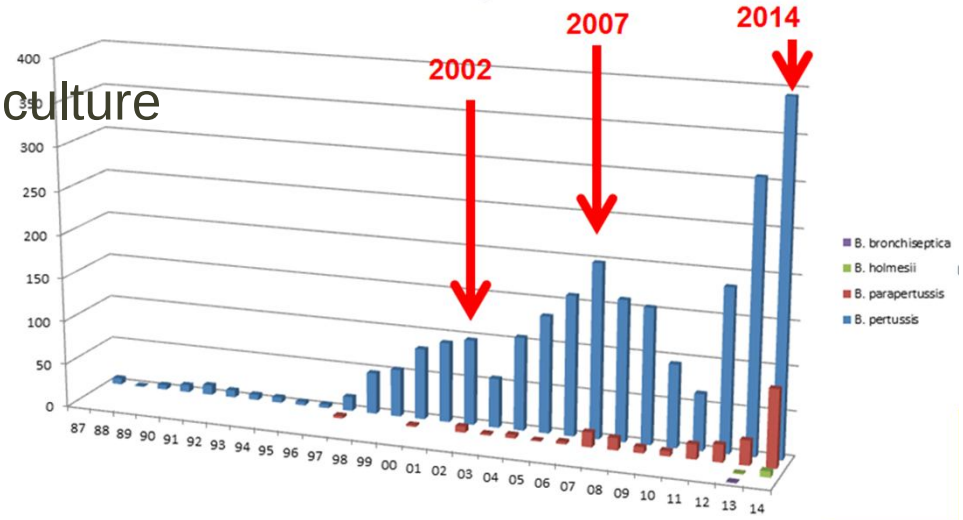


- Possible outcomes:
  - → Positive for *B. pertussis*
  - → Positive for *B. parapertussis*
  - → Positive for *B. holmesii*
  - → Positive for *B. species*, probably *B. pertussis* if compatible with clinical information
  - → Positive for *B. species*, probably *B. parapertussis* if compatible with clinical information
  - → undetermined (weak positive signal, which was not confirmed by repeating the test, sample should be considered as negative)

Results 2014

- **1395 cases of *B. pertussis* infection**
  - → Serology: **930** cases
  - → PCR: **456** cases
  - → Serology + PCR: **7** cases
  - → **2** strains for confirmation by culture
- **94 *B. parapertussis***
- **7 *B. holmesii***





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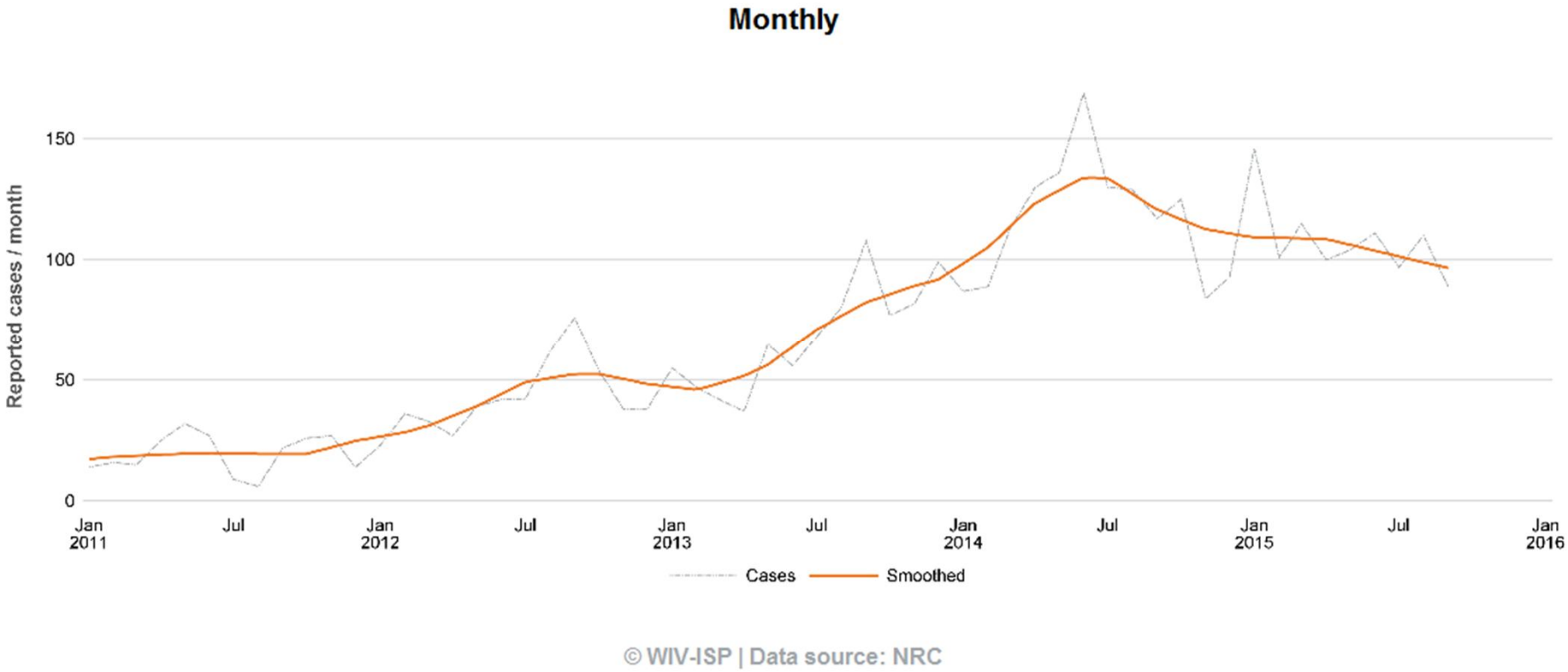
B. pertussis cases reported by the NRC



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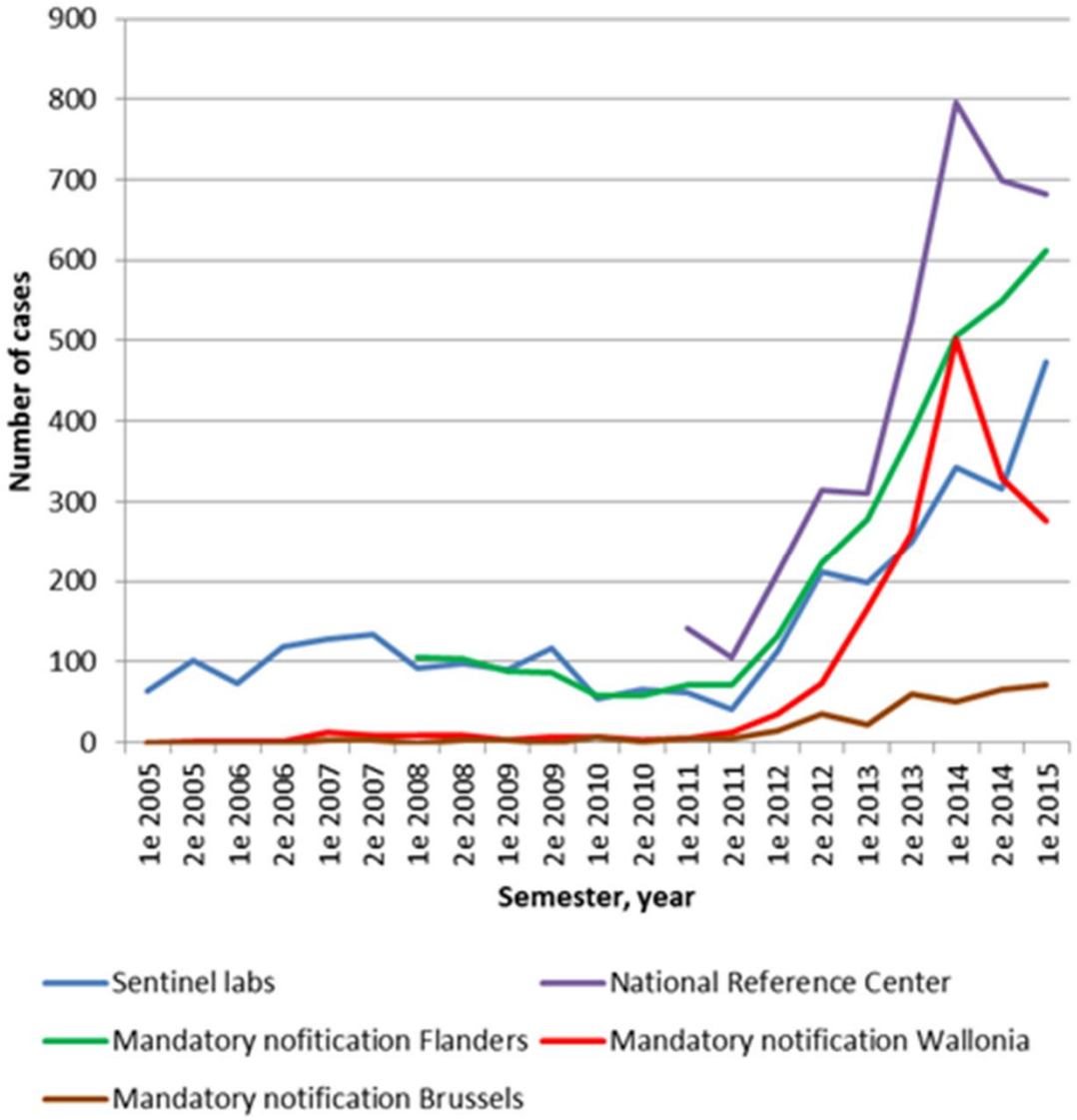
Total number of reported pertussis cases by semester by surveillance system, 2005-2015 (first semester), Belgium.



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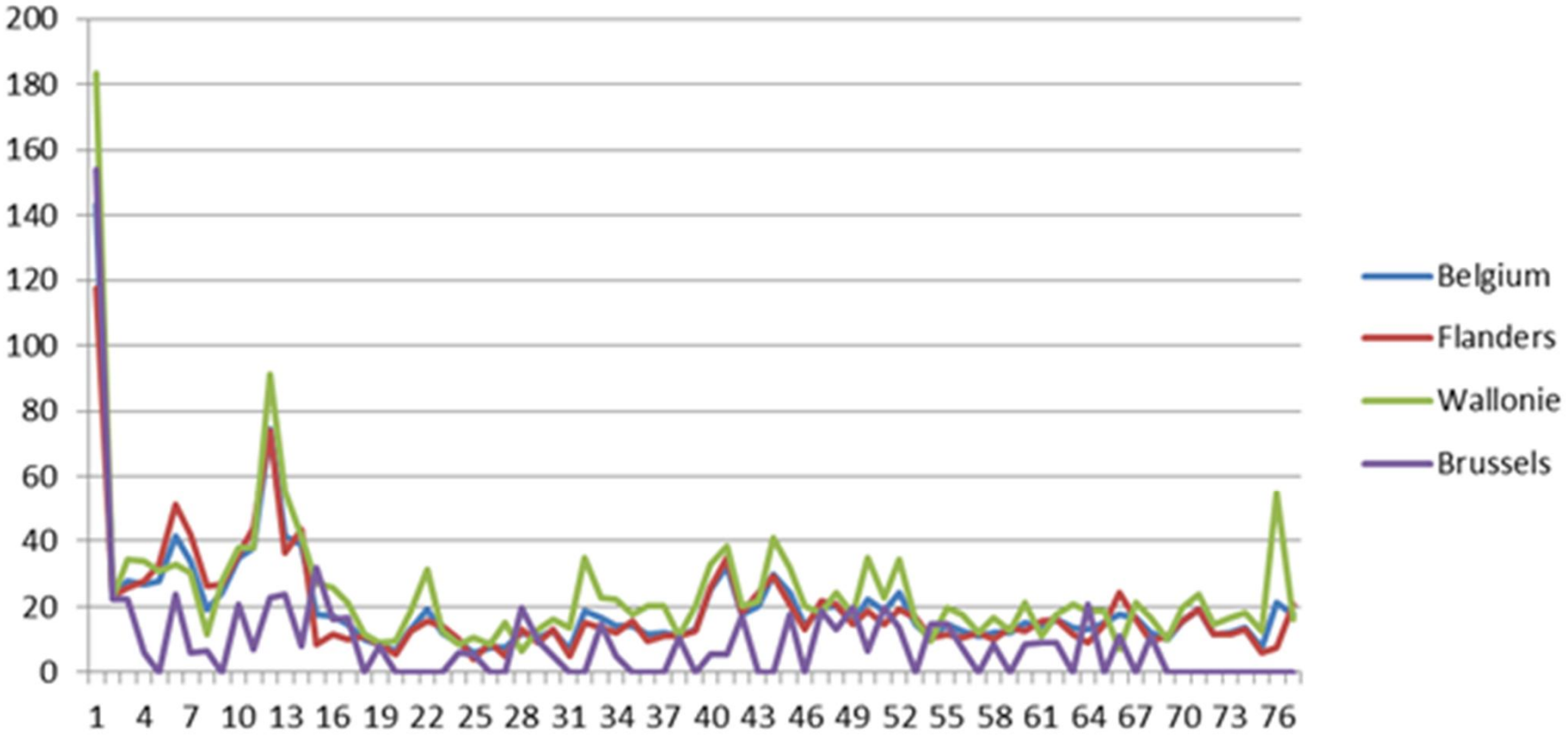
The incidence of the reported pertussis cases by the NRC per region per 100,000, 2014, Belgium (based on 2014 Belgian population data).



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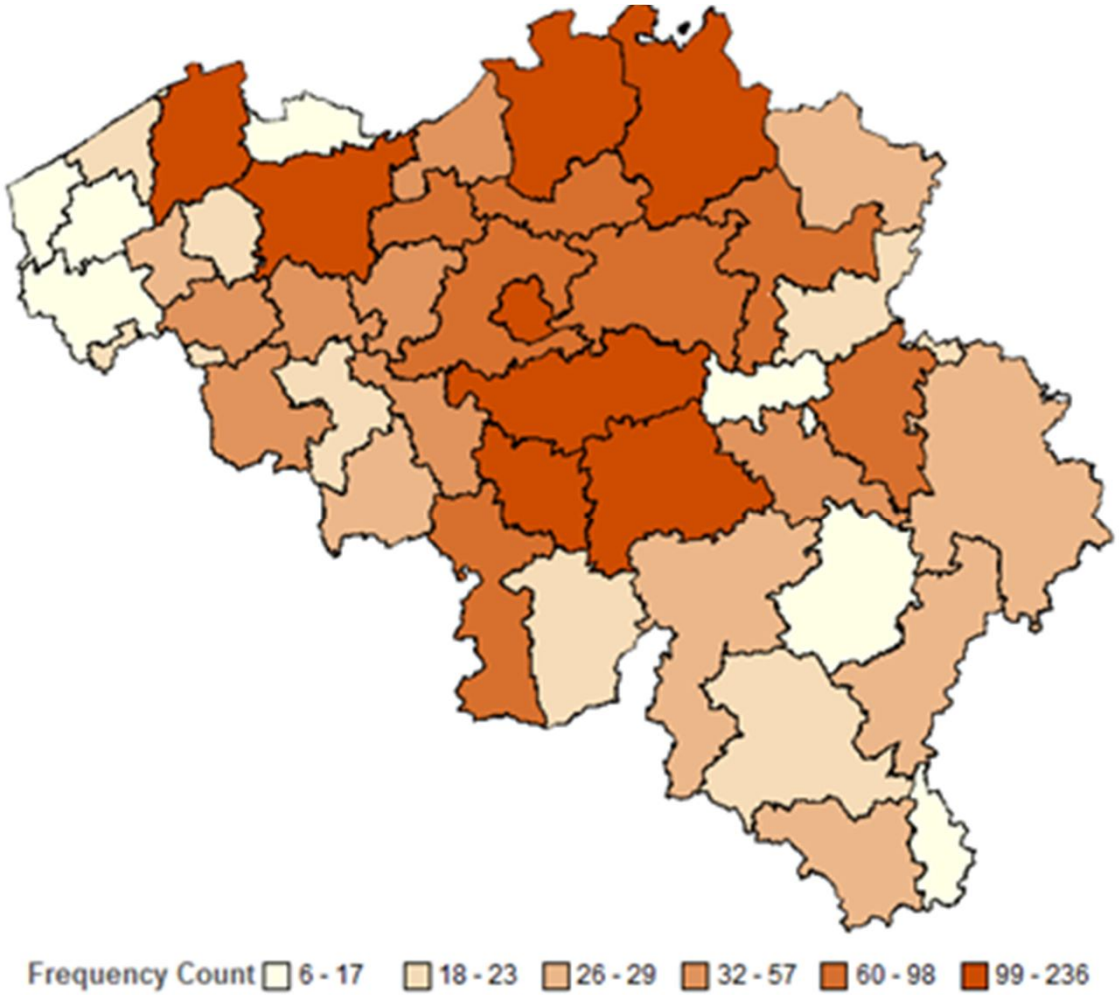
Geographical distribution of reported pertussis cases by borough, 2014, Belgium (NRC, the sentinel laboratory network and the mandatory notification).



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Deaths due to *Bordetella (pertussis)* per age group, 2000-2012, Belgium.

	Mortality data (all *Bordetella* infections)		Minimal Clinical Dataset (*Bordetella pertussis* infections)	
	Number of recorded deaths	Age group (in years)	Number of recorded deaths	Age group (in years)
2000	1	<1	<5	65-74
2001	0	/	0	/
2002	0	/	0	/
2003	0	/	0	/
2004	1	<1	<5	<1
2005	1	<1	<5	45-64
2006	1	<1	0	/
2007	0	/	0	/
2008	0	/	<5	15-19
2009	1	<1	<5	<1
2010	1	<1	<5	<1
2011	2	<1	<5	<1
2012	1	<1	<5	<1

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LE MICROBE DE LA COQUELUCHE

PAR LES Drs J. BORDET ET O. GENGOU

Avec la planche XXVIII.

(Travail de l'Institut Pasteur de Bruxelles.)