Dansk InfektionsPædiatrisk Selskab
Møde, 18 juni 2012

KIGHOSTE - ANNO 2012

Tine Dalby
MSc, PhD

Afd. for Mikrobiologi & Infektionskontrol

STATENS SERUM INSTITUT

HVEM ER JEG?

STATENS SERUM INSTITUT

- Biokemiker af baggrund
- Har været på Statens Serum Institut siden 2003

- Har arbejdet med kighoste siden 2006
- PhD afhandling om kighoste-serologi v. SSI afsluttet i 2010

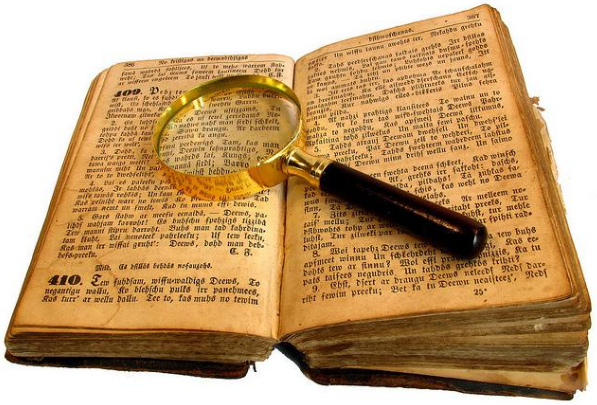
- Nu:
  Forskning og overvågning vedr. kighoste i DK
  Ansvarlig for indsamling af nationale data for lab.påvist kighoste i DK

- Primær dansk repræsentant i den europæiske ekspert-gruppe for kighoste (EuPert)
- Koordinator for flere ECDC-projekter i EuPert regi

OVERSIGT

STATENS SERUM INSTITUT

- **Kighoste brush-up**
  - Hvad er kighoste
  - Hvem får kighoste
  - Hvad er symptomerne på kighoste
  - Hvordan behandles kighoste
  - Kighoste og vaccination
  - Hvordan påvises kighoste



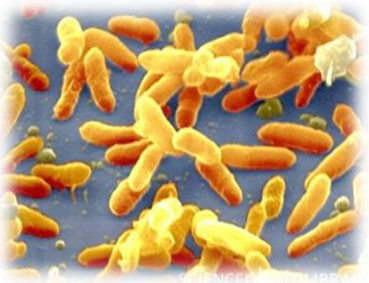
- **Kighoste i Danmark og internationalt**

- **Kighoste i fremtiden**

HVAD?

STATENS SERUM INSTITUT

- Bakterieinfektion : *Bordetella pertussis*.
- Gram-negativ bakterie, ses kun humant



SciencePhotoLibrary

Species	Vært / kilde	Sygdom
B. pertussis	human	pertussis
B. parapertussis	human / får	mild pertussis / pneumoni
B. bronchispetica	pattedyr (hunde)	luftvejsinfektion (kennelhoste)
B. holmesii	human	septicemia, hoste
B. avium	fugle	rhinotracheitis
B. trematum	(human)	Sår, otitis media
B. hinzii	fjerkræ, human	opportunistisk
B. petrii	omgivelser, human	opportunistisk
B. ansorpii	human	opportunistisk

Mooi FR *et al.* Chapter 2 , Bordetella Molecular Microbiology. Camille Locht. (ed) Horizon bioscience 2007

HVEM?

STATENS SERUM INSTITUT

- Myter i befolkningen

Kighoste er kun en børnesygdom

Er man vaccineret, så kan man aldrig få kighoste

Har man haft kighoste før, så kan man aldrig få kighoste igen

HVEM?

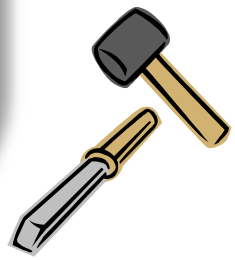
STATENS SERUM INSTITUT

- Sandheden

Kighoste kan ramme alle aldersgrupper

Vaccination beskytter 5-10 år

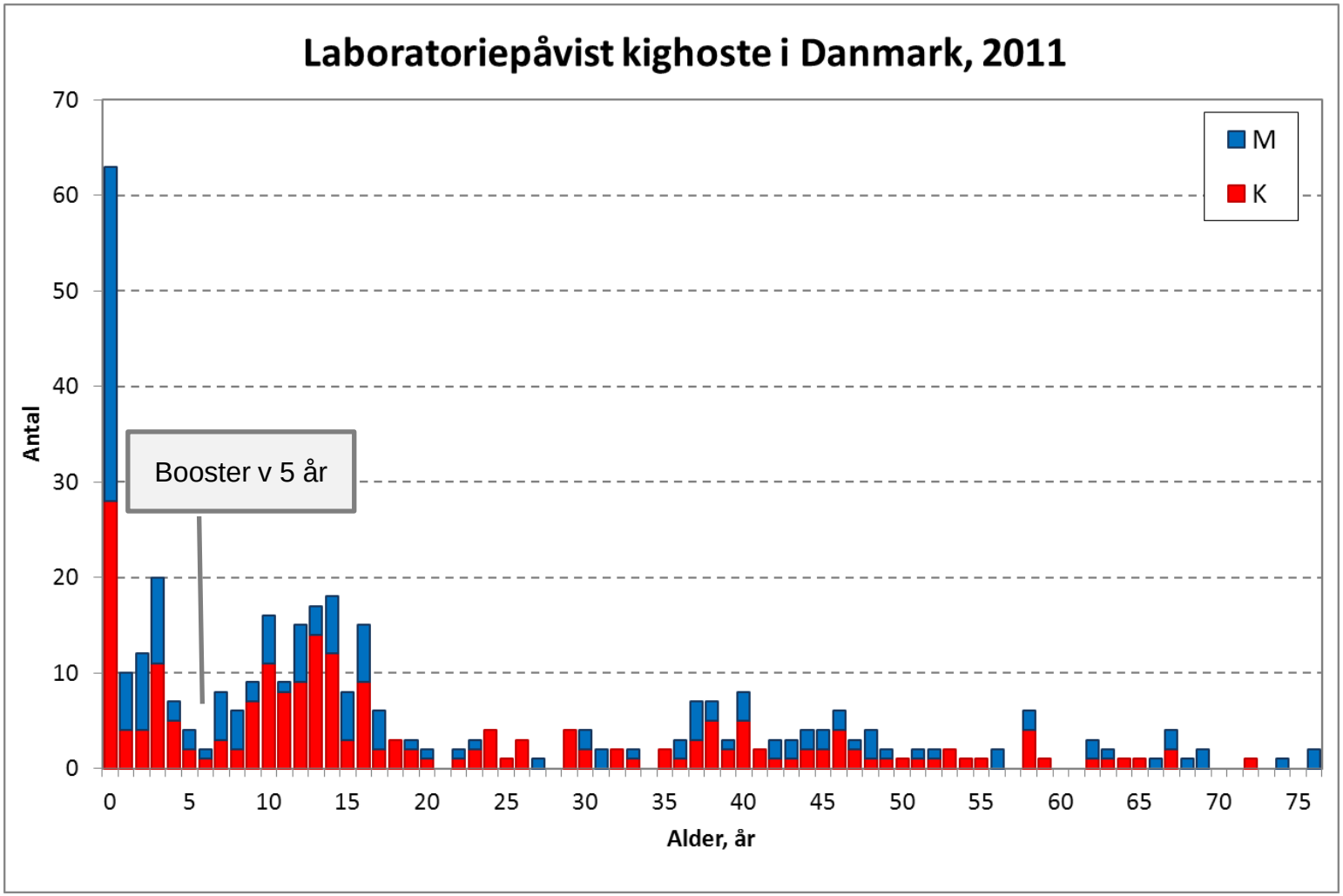
Episode af kighoste beskytter mod re-infektion i 5-10 år



HVEM?

STATENS SERUM INSTITUT

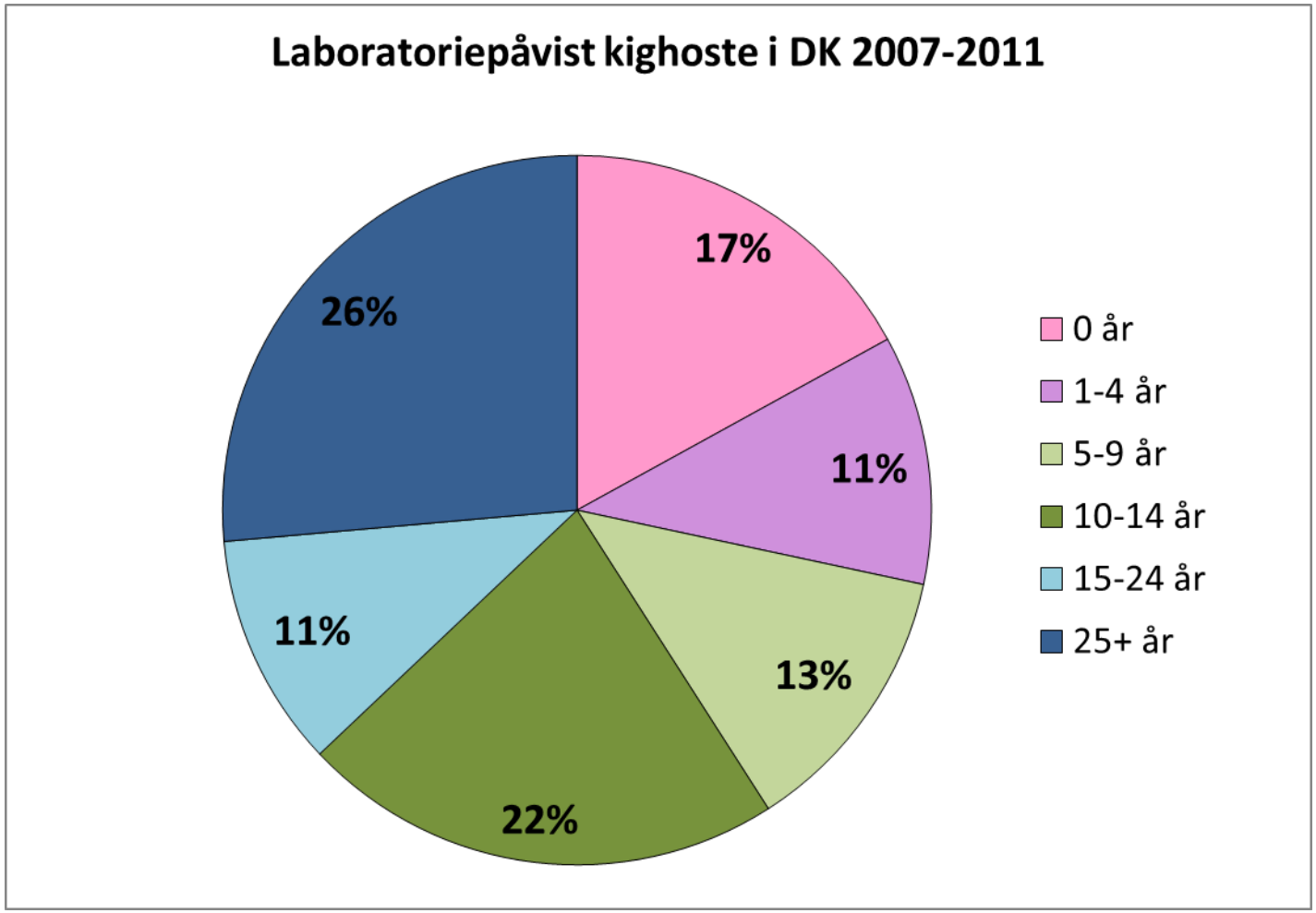
- Kighoste ses i alle aldersgrupper



HVEM?

STATENS SERUM INSTITUT

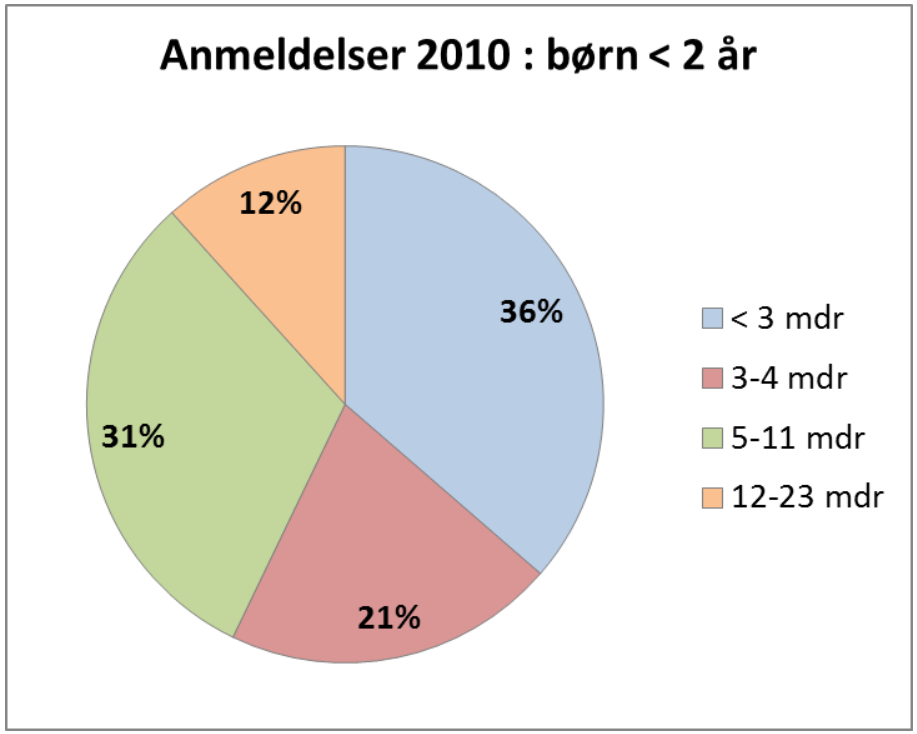
- En stor del af det påviste er fra voksne

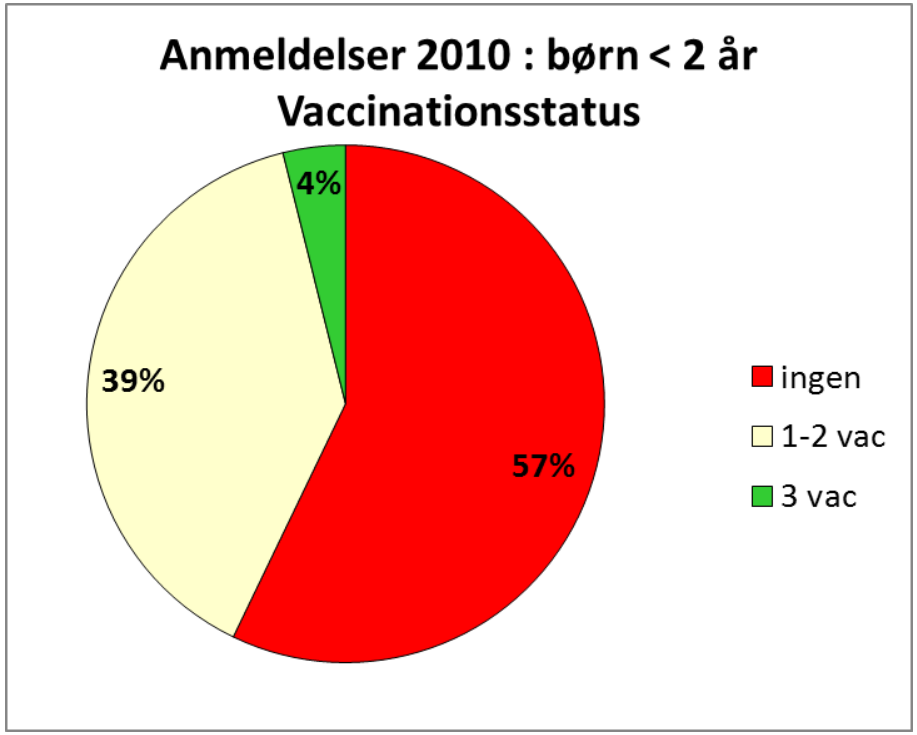


HVEM?

STATENS SERUM INSTITUT

- Kighoste er anmeldelsespligtig for børn under 2 år
- De fleste cases er fra ikke-vaccinerede





EPI-NYT, uge 42-43, 2011

SYMPTOMER

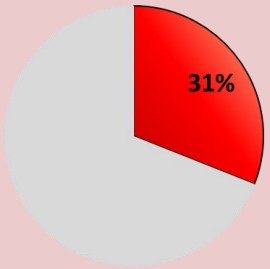
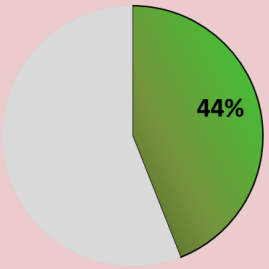
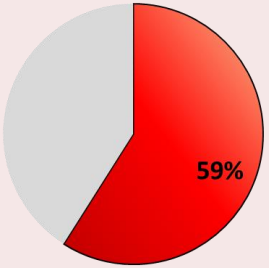
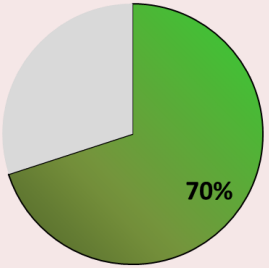
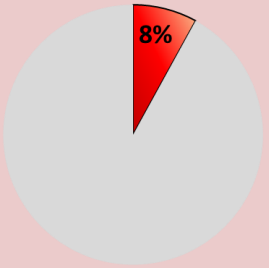
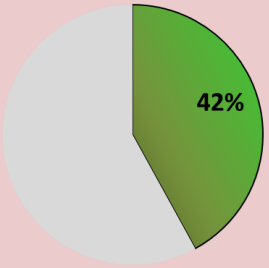
STATENS SERUM INSTITUT

- **Mindre børn** : Klassiske symptomer m. paroxysmer, kigen og opkast
- **Spædbørn** : evt. apnø og cyanose uden regulær hoste

- **Atypisk kighoste**
  - Langvarig hoste uden kigen, uden opkastninger.
  - Jo kortere tid siden vaccination / tidligere kighoste : jo mildere symptomer
  - Mest v. unge og voksne

SYMPTOMER

STATENS SERUM INSTITUT

	Antal og alder	Kigen	Opkast
USA 1989-1998 (Yih *et al*, J.Infect.Dis 2000:182)	3255 patienter unge+voksne		
Canada 1998 (De Serres *et al*, J.Infect.Dis 2000:182)	331 patienter 18-49 år		
Tyskland 1992-94 (Postels-Multani *et al*, Infection 1995:23)	79 patienter voksne		

SYMPTOMER

STATENS SERUM INSTITUT

Generelt

- vægttab og søvnmangel

Komplikationer

- pneumoni
- otitis media
- subconjunctival blødning
- brok (imbulical, abdominal, inguinal)
- temporær urin-inkontinens
- brækkede ribben

Hewlett EL. in Mandell GL, Bennett JE, Dolin R, editors. Principles and Practice of Infectious Diseases. 5 ed. Philadelphia: Churchill Livingstone; 2000; 219, Bordetella Species. p. 2414-22.

Halperin SA. in Kasper, Braunwald, Fauci, Hauser, Longo, Jameson, editors.Harison's Principles of Internal Medicine. 16 ed. McGraw-Hill Professional; 2005; 133, Pertussis and other bordetella infections. p. 874-7.

SYGEHISTORIER

STATENS SERUM INSTITUT

The patient developed a mild cough. After 2 weeks a colleague suggested she see a physician because the cough was annoying him. This began the first of about half a dozen visits to her physician. Her physician thought it was nothing or **asthma**, but she was concerned about a **tumor**. Paroxysms were so bad she slept sitting up and outside. She could not catch her breath and had urinary incontinence with paroxysms. Her chest hurt so bad that she suspected a broken rib. After 6 weeks, her research leader called me and I noted classic cough, which was confirmed by serologic testing. Her illness **lasted 3 months**.

The patient became ill with an afebrile illness with severe paroxysmal cough. He was seen by an otorhinolaryngologist and an internist. Chest and sinus x-ray findings were normal. His "choking episodes" were severe. He was treated with **steroids**, and **antihistamine**, a **tranquilizer**, and subsequently **amoxicillin**. The patient was seen by 3 physicians and the diagnoses were "uniformly vague." The patient's wife developed the same illness 2 weeks after its onset in the patient. At the time of a well-child visit the UCLA pediatrician diagnosed pertussis in the patient and his wife and this diagnosis was confirmed by serologic testing. The patient's illness **lasted 11 weeks**.

Onset of cough illness occurred on 15 July, and a sweating episode occurred on 18 July. On 29 July, his first whooping episode occurred, and he was treated with azithromycin. An internist diagnosed "**cough variant asthma**" on 3 August and decided to rule out **insulinoma**; the patient was treated with **prednisone**. On 7 August, an otorhinolaryngologist diagnosed **Wegener granulomatosis**, and the patient underwent **CT of the head and neck**. Positive PCR results were obtained on 14 August. **From August through October,** coughing continued, without improvement.

Cherry JD, 2010, CID 2010:51

HVEM SMITTER?

STATENS SERUM INSTITUT

- Kighoste er den mest smitsomme bakterie-infektion man kender til, og er ligeså smitsom som mæslinger

SOME EPIDEMIOLOGICAL PROPERTIES OF VACCINE-PREVENTABLE CHILDHOOD VIRAL AND BACTERIAL INFECTIONS

Infection/ infectious agent	Average age at infection, A (developed countries before immunisation) in yr	Inter-epidemic period (yr)	R_0	Critical vaccination coverage to block transmission p_c *(%)*
Measles	4–5	2	15–17	*92–95*
Pertussis	4–5	3–4	15–17	*92–95*
Mumps	6–7	3	10–12	*90–92*
Rubella	9–10	3–5	7–8	*85–87*
Diphtheria	11–14	4–6	5–6	*80–85*
Polio virus	12–15	3–5	5–6	*80–85*

Anderson RM *et al*, Lancet. 1990 ;335(8690):641-5.

HVEM SMITTER?

STATENS SERUM INSTITUT

- Det er vist i flere tilfælde, at det er voksne der smitter de små børn.
- Dvs. der er ikke primært tale om barn-til-barn transmission!

Results: The study population comprised 95 index cases and 404 contacts. The source of pertussis was identified for 48% of infants in the primary analysis and up to 78% in sensitivity analyses. In the primary analysis, parents accounted for 55% of source cases, followed by siblings (16%), aunts/uncles (10%), friends/cousins (10%), grandparents (6%) and part-time caretakers (2%). The distribution of source cases was robust to sensitivity analyses.
Conclusions: This study provides solid evidence that among infants for whom a source case was identified, household members were responsible for 76%–83% of transmission of *Bordetella pertussis* to this high-risk group. Vaccination of adolescents and adults in close contact with young infants may thus eliminate a substantial proportion of infant pertussis if high coverage rates can be achieved.

Wendelboe *et al*, 2007, Pediatr Infect Dis J, 26(4)

BEHANDLING

WHOOPING COUGH
INSTANTLY RELIEVED
AND
QUICKLY CURED.

CRESOLENE.

PAGE'S
PATENT
VAPOURISER
AND
CRESOLENE.

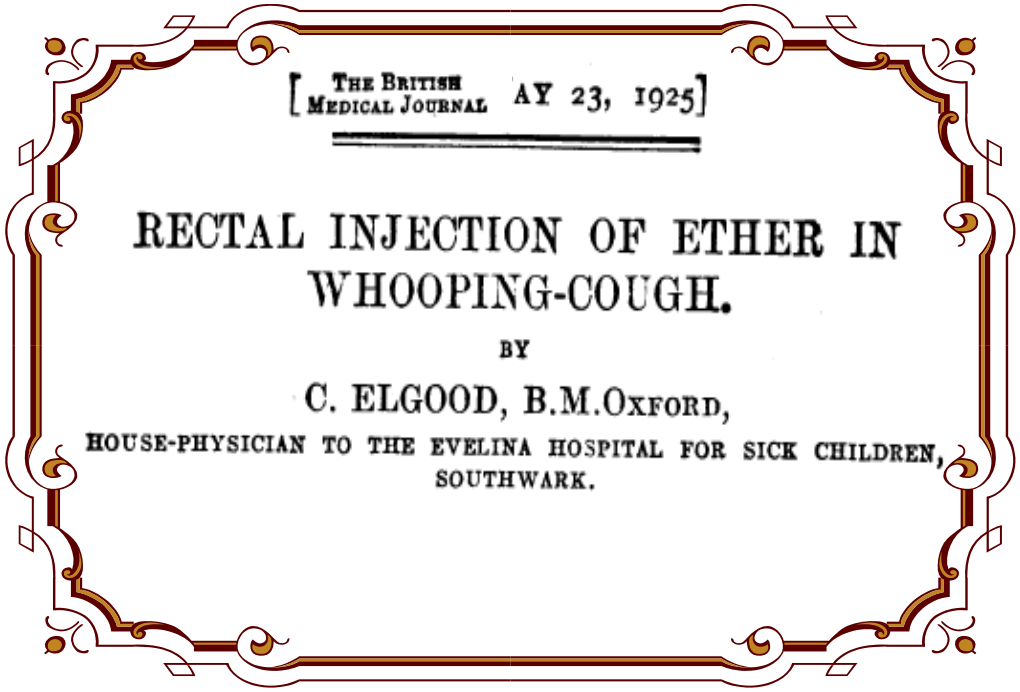
Children, by simply breathing the vapour of Cresolene, ob[illegible] in a few seconds extraordinary relief in Whooping-Cough, and the disorder is rapidly put an end to, generally in a few days. It is a perfectly safe remedy and will not harm the youngest child. CRESOLENE is most valuable in Asthma, Catarrh, Scarlet Fever, Diphtheria, Hay Fever, &c.

CRESOLENE is claimed to be the most powerful antiseptic and disinfectant at present known.

Vapouriser, with Lamp complete, and 2 oz. Bottle of Cresolene, 7s. 6d., post-free in the United Kingdom; or can be obtained through any Chemist. The Cresolene can be had separately, in Bottles, at 1s. 4d. and 2s. 6d. *Sole Agents for Europe:*

ALLEN & HANBURYS, Plough-ct., LONDON.

Ask your Chemist for a Descriptive Circular.



[THE BRITISH MEDICAL JOURNAL AY 23, 1925]

RECTAL INJECTION OF ETHER IN WHOOPING-COUGH.

BY

C. ELGOOD, B.M.OXFORD,

HOUSE-PHYSICIAN TO THE EVELINA HOSPITAL FOR SICK CHILDREN, SOUTHWARK.

BEHANDLING

STATENS SERUM INSTITUT

- Behandling af selve hosten

Symptomatic treatment of the cough in whooping cough (Review)

Bettiol S, Thompson MJ, Roberts NW, Perera R, Heneghan CJ, Harnden A

THE COCHRANE COLLABORATION®

Main results

....
Diphenhydramine did not change coughing episodes;
the mean difference of coughing spells per 24 hours was 1.9.
One study on pertussis immunoglobulin reported a possible mean reduction of -3.1 whoops per 24 hours but no change in hospital stay.
Dexamethasone did not show a clear decrease in length of hospital stay.
Salbutamol showed no change in coughing paroxysms per 24 hours.

Authors' conclusions

Insufficient evidence exists to draw conclusions about the effects of interventions for the cough in whooping cough.

BEHANDLING

STATENS SERUM INSTITUT

- Antibiotika-behandling

Antibiotics for whooping cough (pertussis) (Review)

Altunaiji S, Kukuruzovic R, Curtis N, Massie J

THE COCHRANE COLLABORATION®

Main results

...

Short-term antibiotics (azithromycin for three to five days, or clarithromycin or erythromycin for seven days) were as effective as longterm (erythromycin for 10 to 14 days) in eradicating *Bordetella pertussis* from the nasopharynx but had fewer side effects. Trimethoprim/sulfamethoxazole for seven days was also effective. Nor were there differences in clinical outcomes or microbiological relapse between short and longterm antibiotics.

Contact prophylaxis of contacts older than six months of age with antibiotics did not significantly improve clinical symptoms or the number of cases developing culture-positive *B. pertussis*.

Authors' conclusions

Although antibiotics were effective in eliminating *B. pertussis*, they did not alter the subsequent clinical course of the illness.

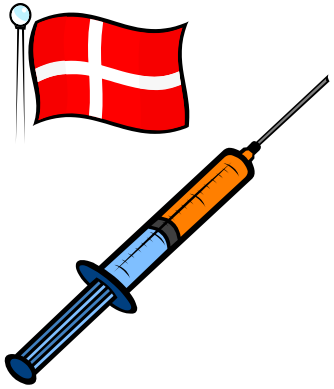
There is insufficient evidence to determine the benefit of prophylactic treatment of pertussis contacts.

VACCINATION

VACCINATION

STATENS SERUM INSTITUT

- De danske anbefalinger
  - 3 mdr
  - 5 mdr
  - 12 mdr
  - 5 år, booster (2003)



- Småbørnsvaccine DiTeKiPol/Act-Hib
- Booster vaccine DiTeKiPol Booster

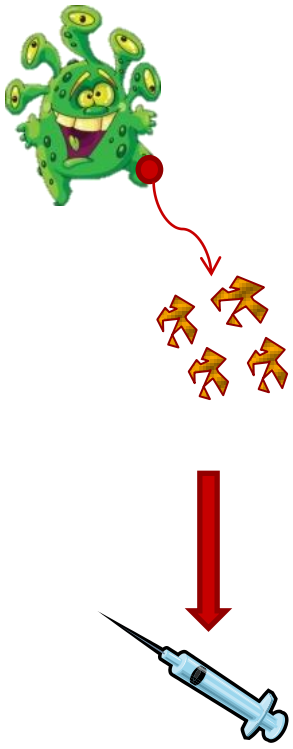
VACCINATION

STATENS SERUM INSTITUT

- Den danske vaccine indeholder kun et toxin fra *B. pertussis*. Bivirkninger, som ved den tidligere helcelle-vaccine ,er minimerede.

Før1997 : wP

Fra1997 : aP



VACCINATION

STATENS SERUM INSTITUT

- Beskyttelse mod kighoste v småbørnsvaccinationerne i Danmark

- Data for børn 0-2 år

EFFECTIVENESS	Anmeldelser	Indlæggelser
0 doser	0 %	0 %
1 dosis	35 %	37 %
2 doser	59 %	72 %
3 doser	78 %	93 %

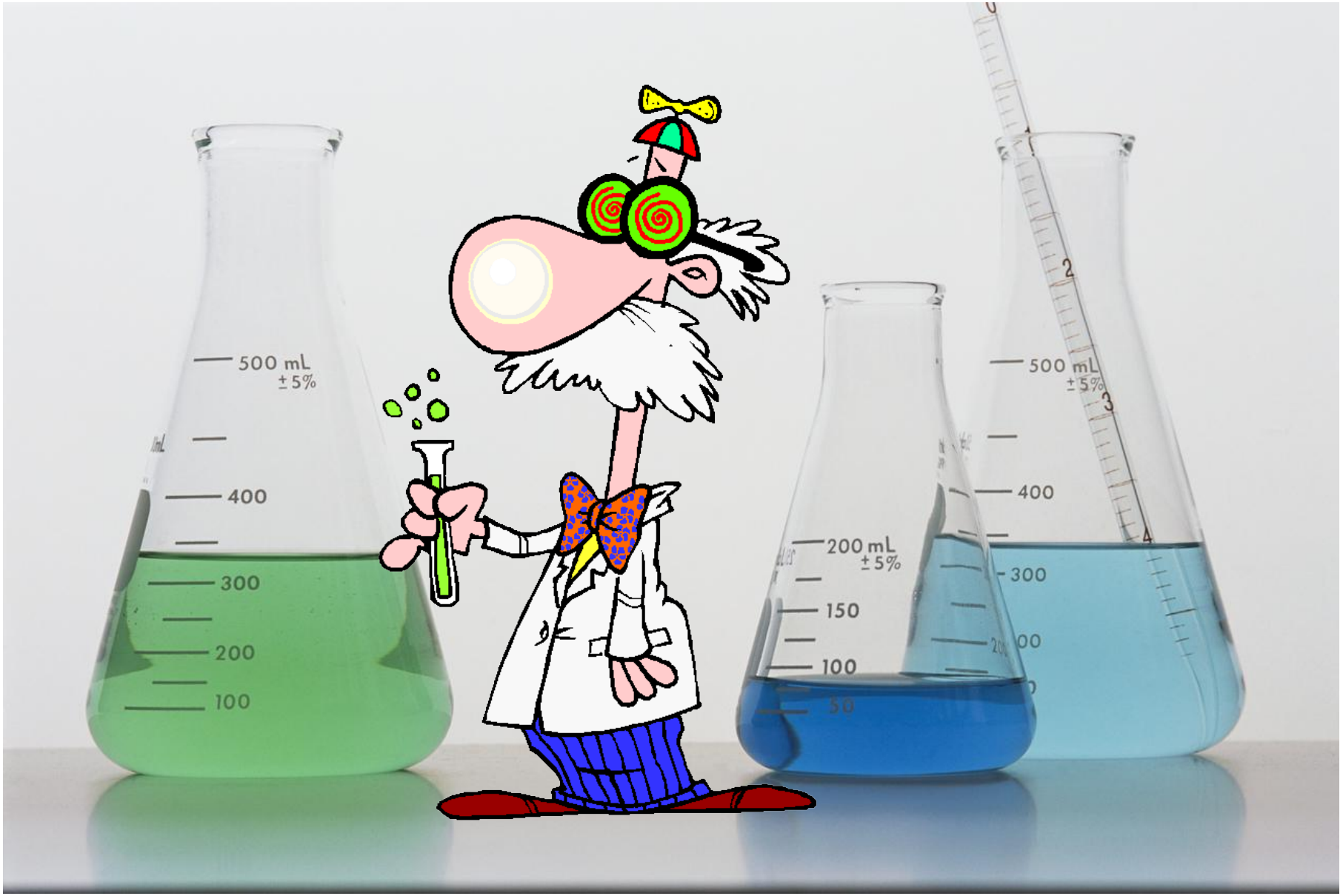
Impact of routine vaccination with a pertussis toxoid vaccine in Denmark

Anders Hviid[a,*], Michael Stellfeld[b], Peter Henrik Andersen[c], Jan Wohlfahrt[a], Mads Melbye[a]

Vaccine

PÅVISNING I LABORATORIET

STATENS SERUM INSTITUT



PÅVISNING I LABORATORIET

STATENS SERUM INSTITUT

- Kighoste kan påvises ved:

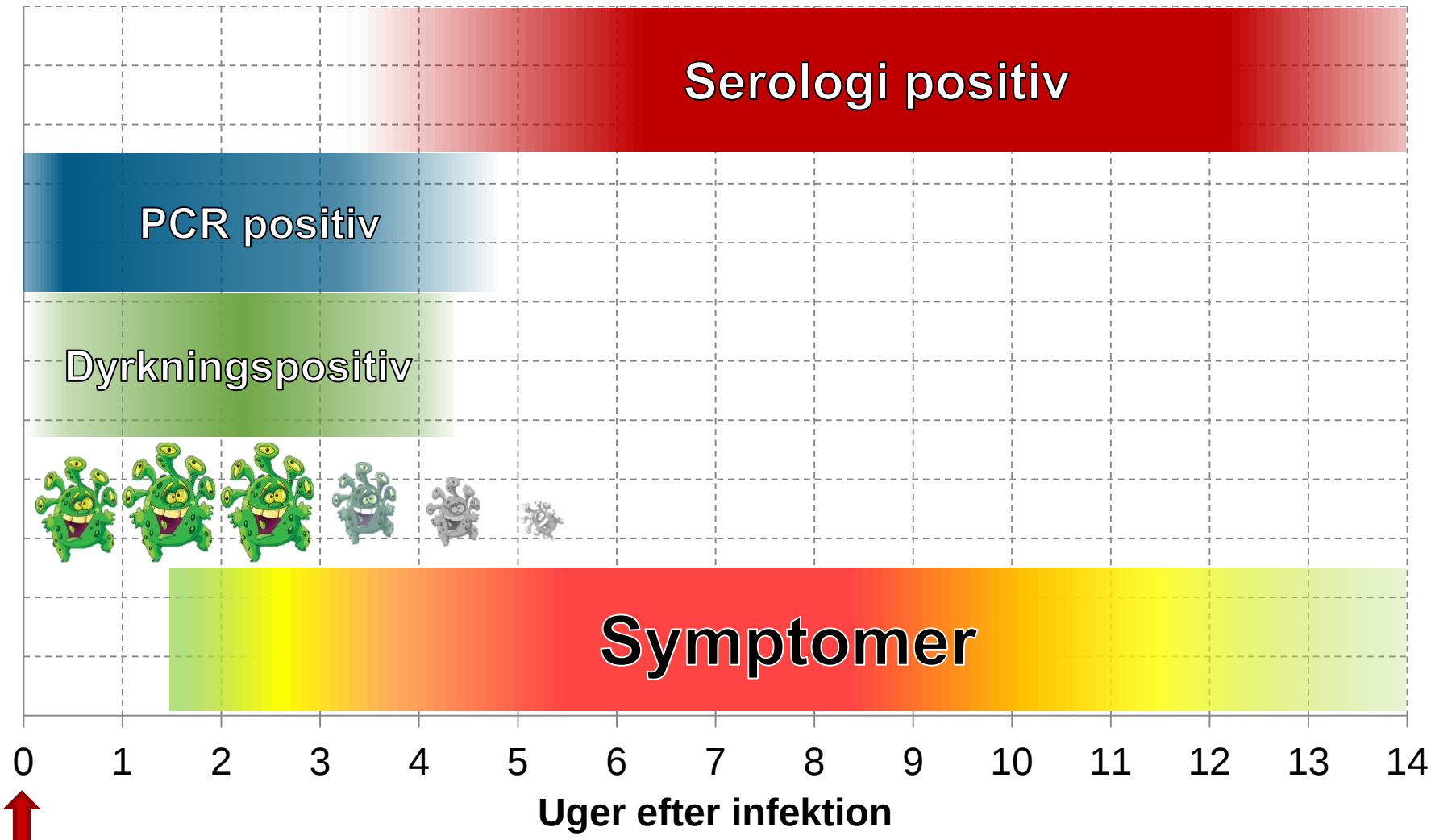
Dyrkning

PCR

Serologi

PÅVISNING I LABORATORIET

STATENS SERUM INSTITUT



Tidspunkt for smitten

PÅVISNING I LABORATORIET

STATENS SERUM INSTITUT

- Prøvetagning mht. sygdomsvarighed, opsummering:

Dyrkning

ca. ved smittetidspunkt ⇔2-3 uger med symptomer
Ikke anvendelig v antibiotika-behandling
Vigtig mht. overvågning af bakterie-populationen!

PCR

ca. ved smittetidspunkt ⇔ 3-4 uger med symptomer

Serologi

Fra 2 uger med symptomer ⇔ 3-6 måneder
Vaccinationsantistoffer holder i ca. 2 år
Anbefales fra 8 år (ellers > 2 år efter vaccination)

PÅVISNING I LABORATORIET

STATENS SERUM INSTITUT

Voksne søger oftest læge sent, efter nogle uger med hoste

↓

PCR er ofte negativ, også selvom patienten faktisk <u>har</u> pertussis

↓

Serologi bør anvendes!

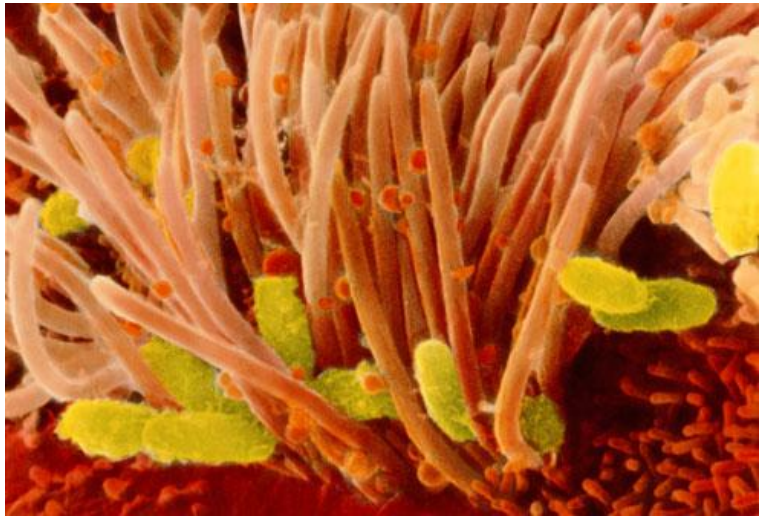
PÅVISNING I LABORATORIET

STATENS SERUM INSTITUT

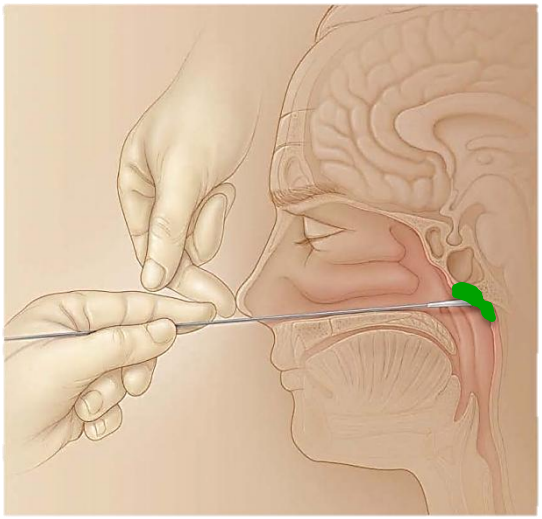
Prøvetagning til PCR eller dyrkning

- Bakterien adhederer til cilieret epithel i nasopharynx

- Prøven **SKAL** være podning eller aspirat fra nasopharynx, ikke næse / svælg / sputum / ekspektorat



http://children.webmd.com/pertussis-whooping-cough-10/slideshow-prevent-pertussis

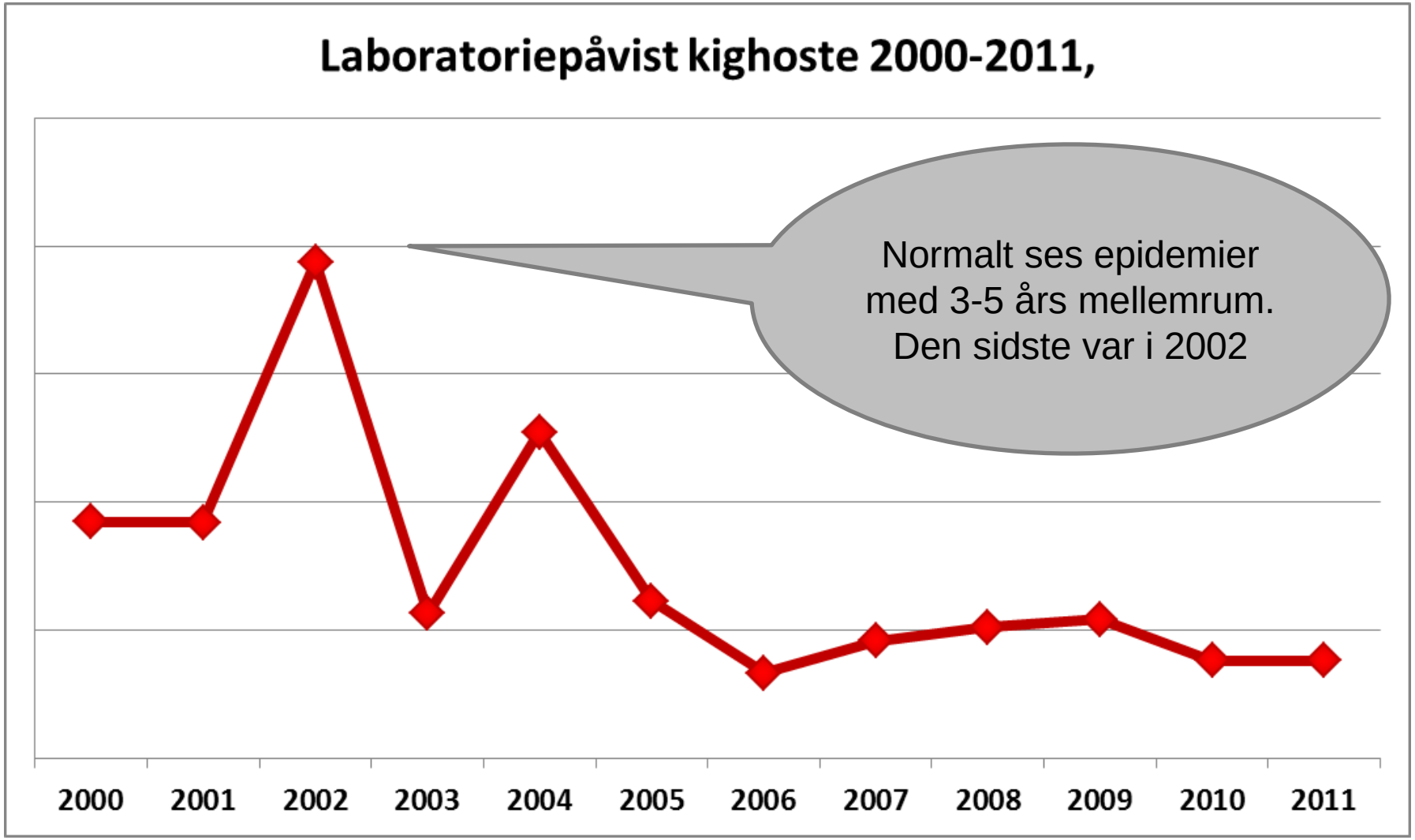


KIGHOSTE I DANMARK

NASA

KIGHOSTE I DANMARK

STATENS SERUM INSTITUT



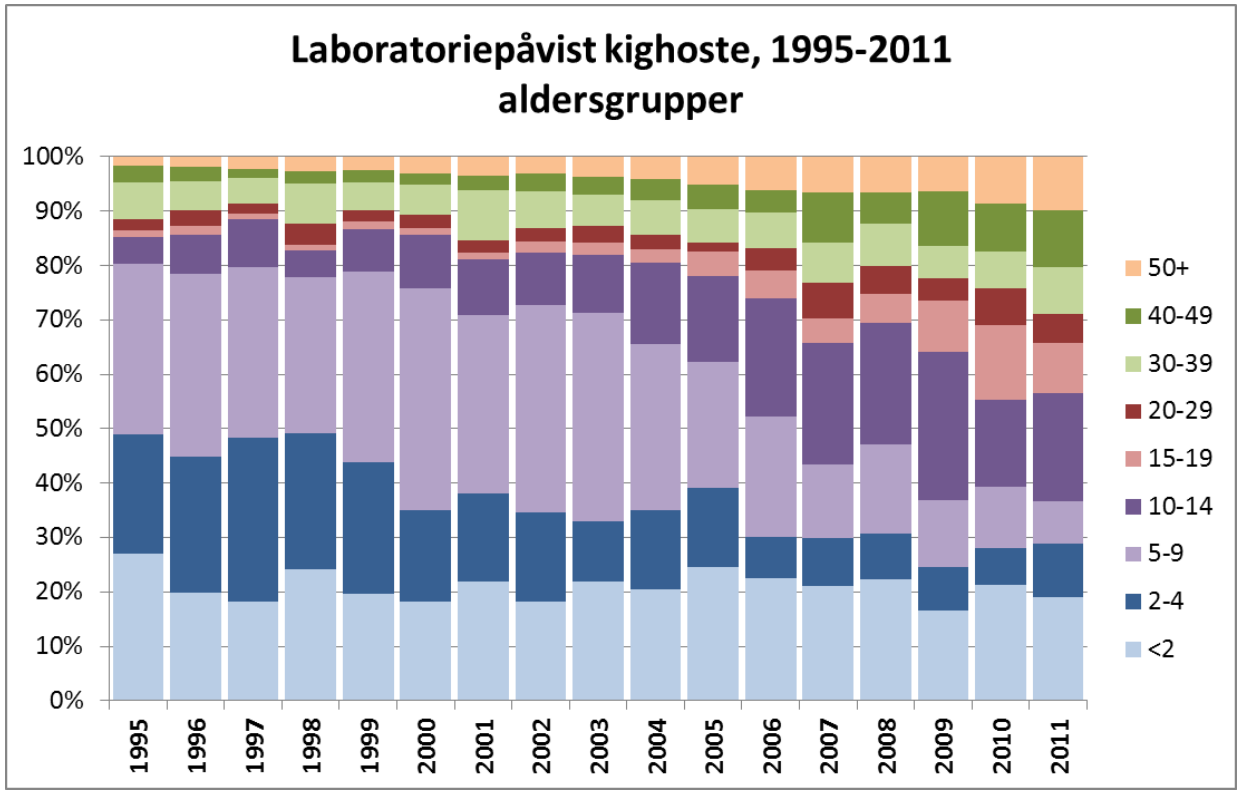
KIGHOSTE I DANMARK

STATENS SERUM INSTITUT

KIGHOSTE I DANMARK

STATENS SERUM INSTITUT

- **Skift i aldersfordeling**
  - fald for 5-9 årige pga. boostervaccinen, indført 2003
  - stigning for 10-19 årige pga faldende immunitet efter boosteren
  - stigning hos de voksne pga øget kendskab og bedre diagnostik



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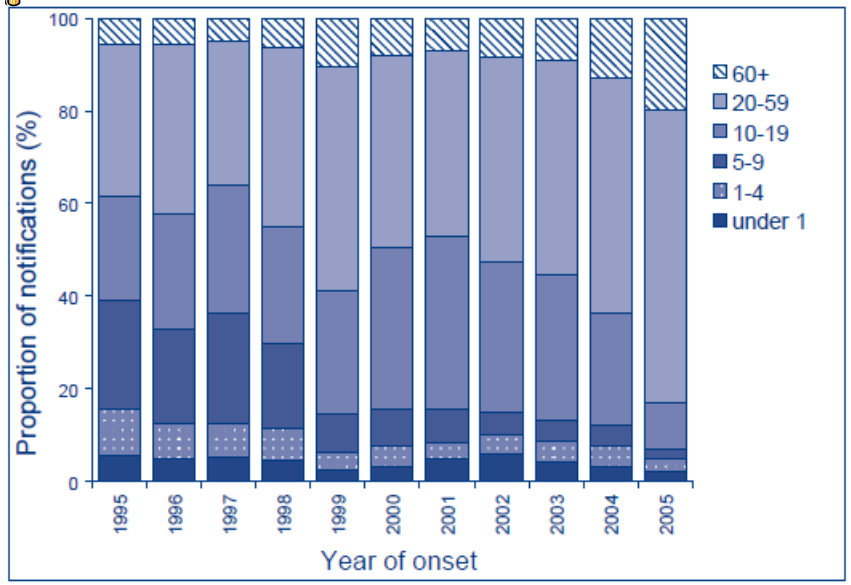
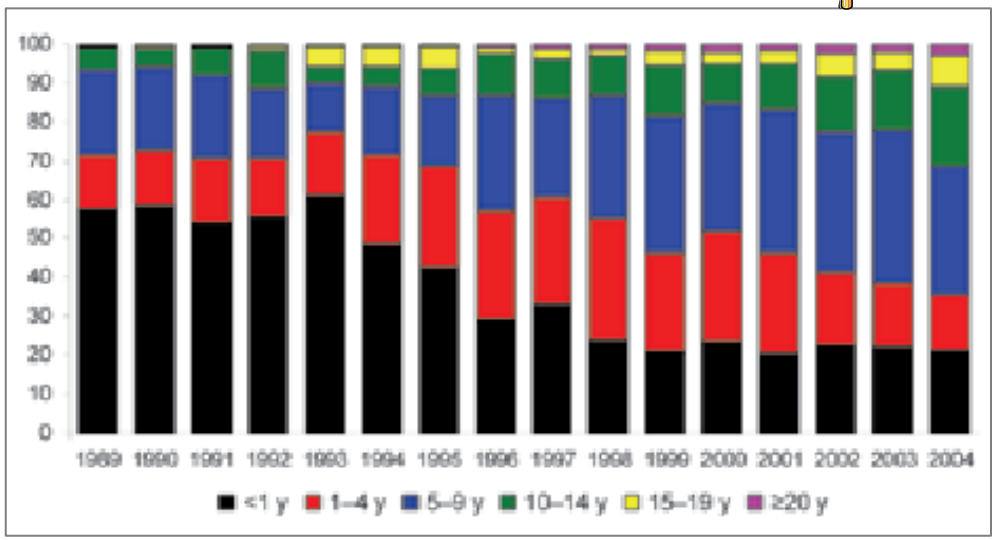


Quinn *et al* Commun Dis Intell 2007:31(2)



Mooi *et al* Emerg Infect Dis 2009:15(8)

KIGHOSTE I DANMARK

STATENS SERUM INSTITUT

- 2012

EPI-NYT

Udvalgte laboratoriepåviste infektioner

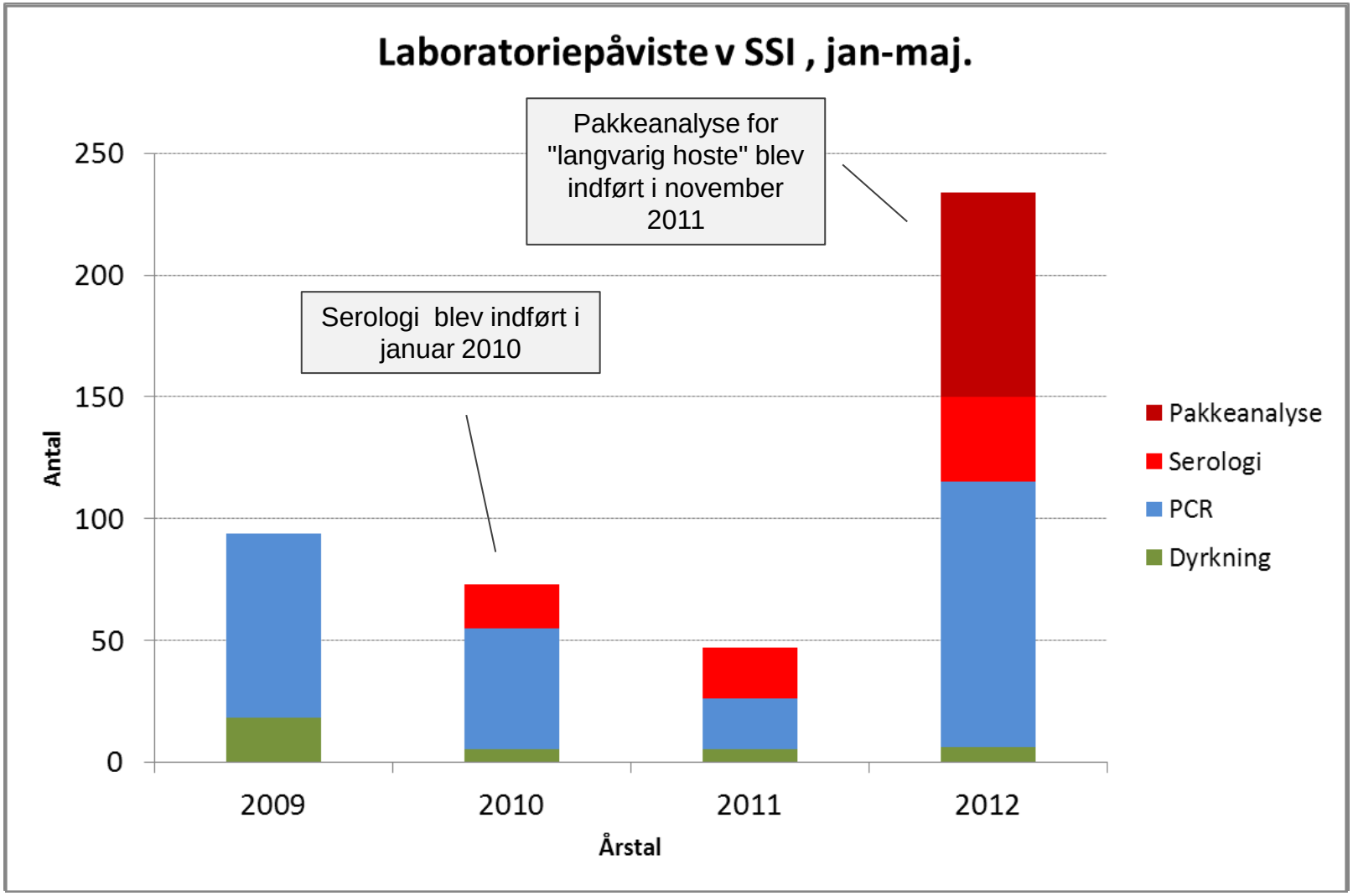
Antal prøver, isolater og/eller anmeldelser modtaget i laboratorier, Statens Serum Institut.

Tabel 2	Uge 23 2012	Kum. 2012 [2)]	Kum. 2011 [2)]
Bordetella pertussis (alle aldre)	12	228	42

Hov! Hvad er nu det?

KIGHOSTE I DANMARK

STATENS SERUM INSTITUT

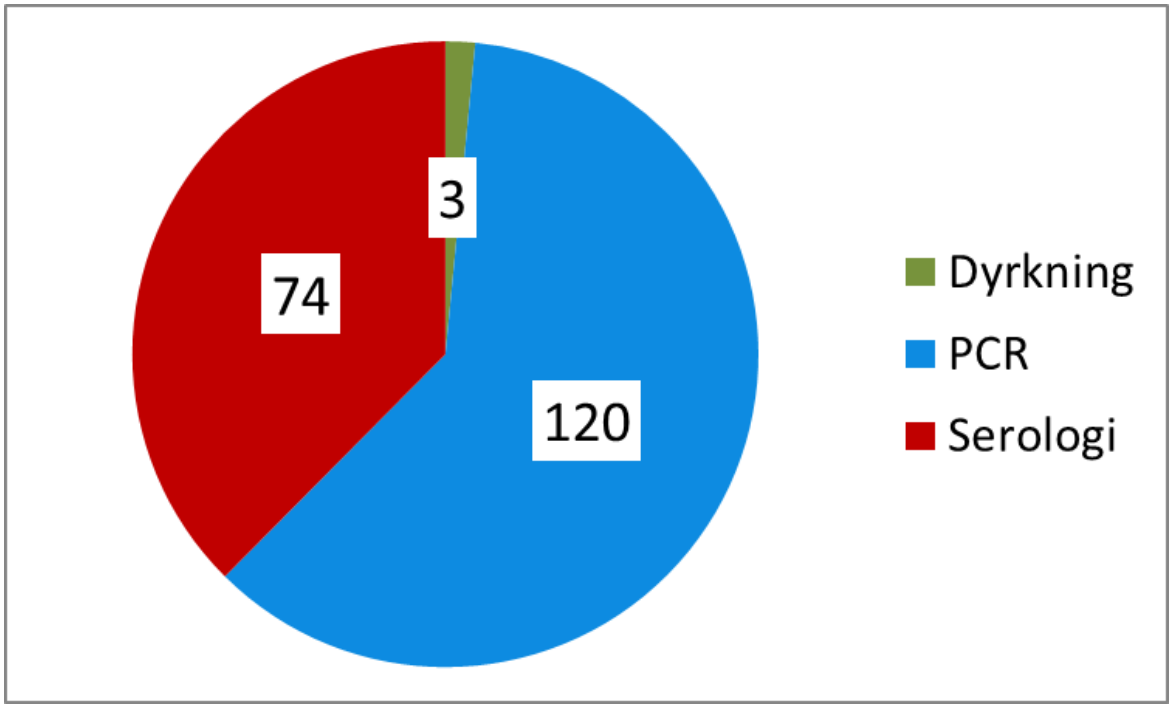


KIGHOSTE I DANMARK

STATENS SERUM INSTITUT

- Påvist kighoste i Danmark, 1 kvartal 2012

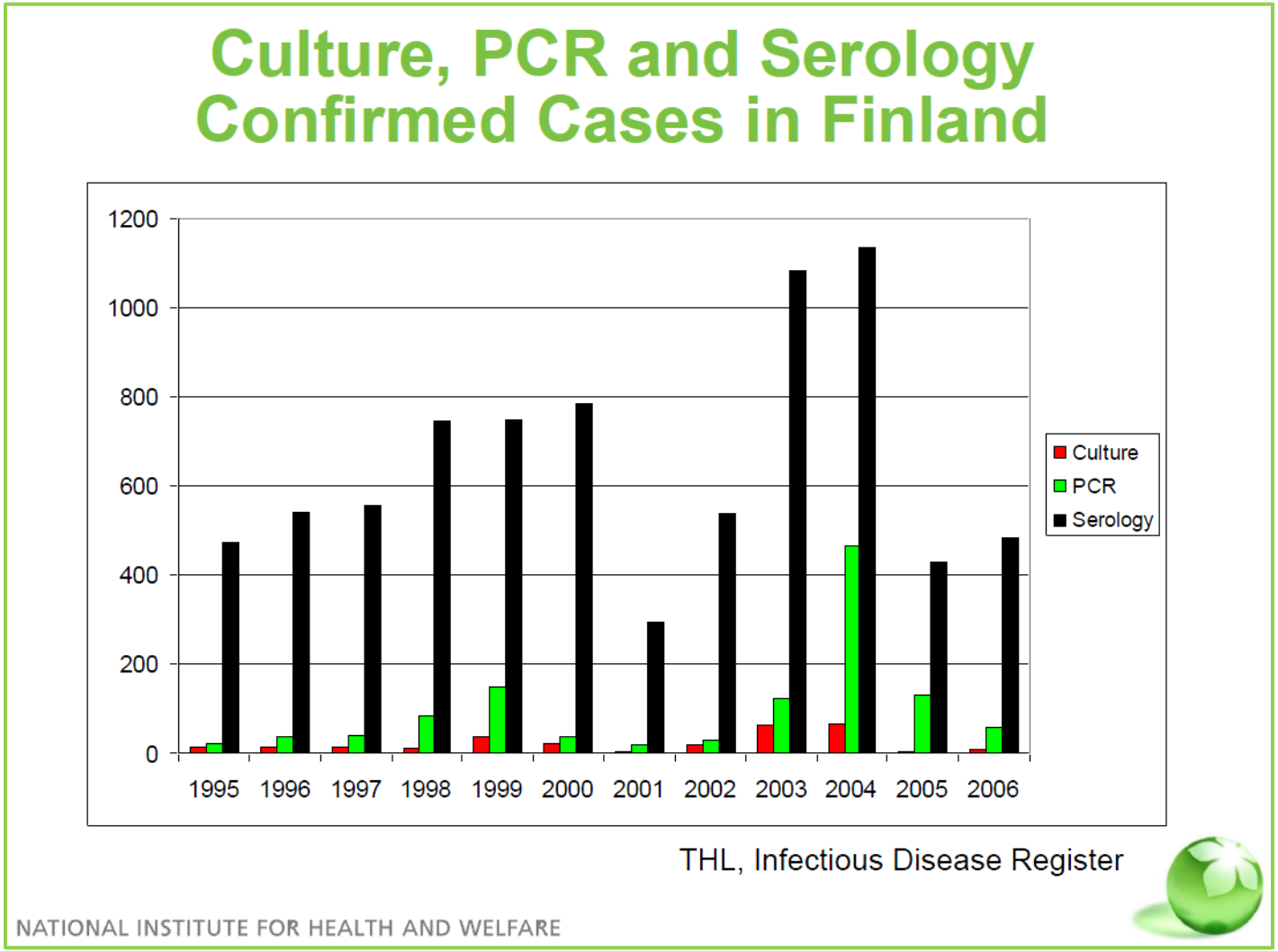
  (SSI, Herlev, Hvidovre, Odense, Viborg, Skejby. Serologi: kun SSI)



KIGHOSTE I DANMARK

STATENS SERUM INSTITUT

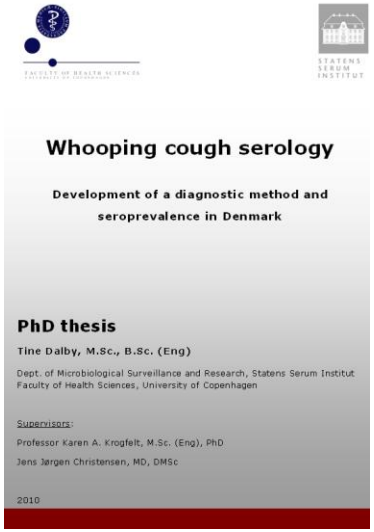
- Påvist kighoste i Finland (THL, Turku: Dr. Qiushui He)



KIGHOSTE I DANMARK

STATENS SERUM INSTITUT

- Serologi: Høj specificitet og høj sensitivitet
- Ingen kendte krydsreaktioner
- Anvendelig >2 år efter vaccination


Whooping cough serology

Development of a diagnostic method and seroprevalence in Denmark

PhD thesis

Tine Dalby, M.Sc., B.Sc. (Eng)

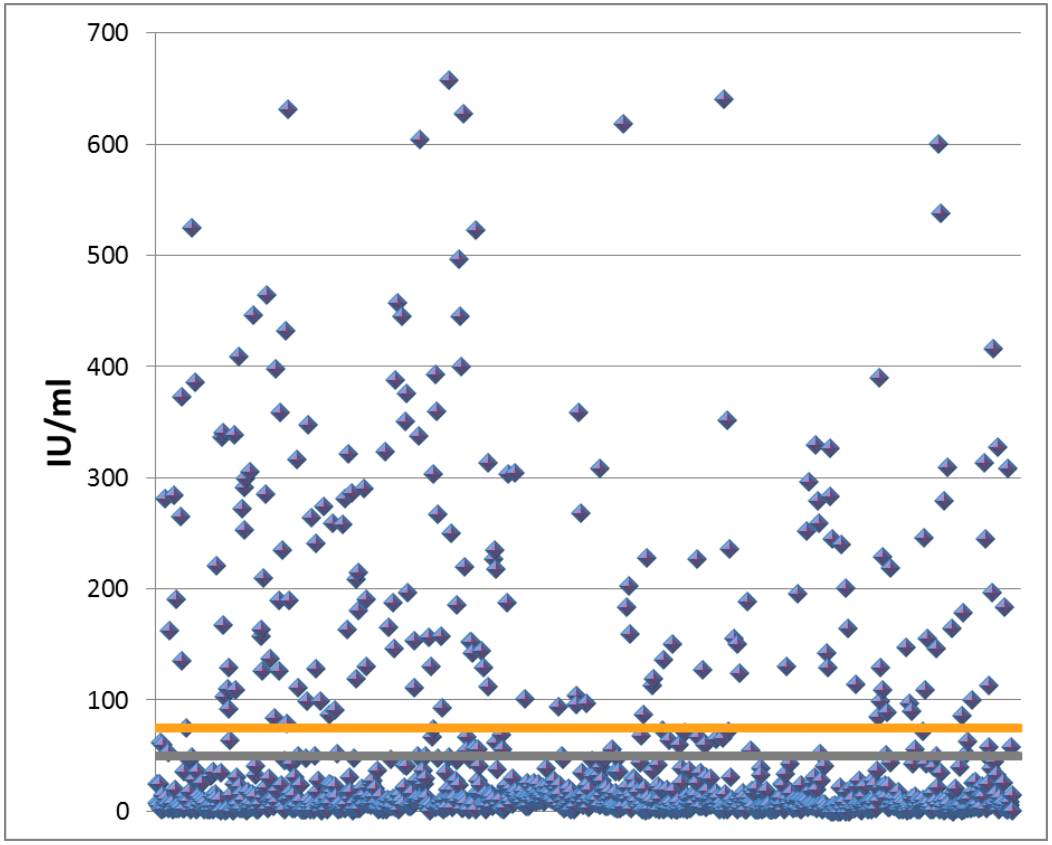
Dept. of Microbiological Surveillance and Research, Statens Serum Institut
Faculty of Health Sciences, University of Copenhagen

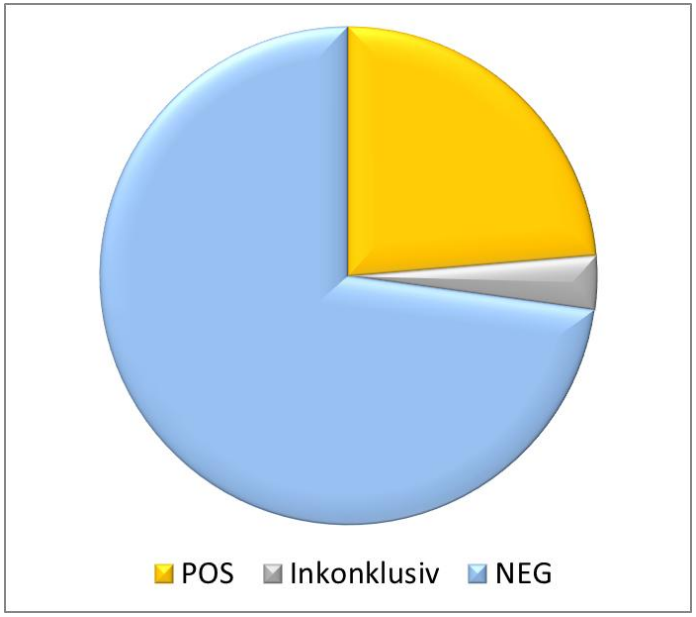
Supervisors:

Professor Karen A. Krogfelt, M.Sc. (Eng), PhD

Jens Jørgen Christensen, MD, DMSc

2010





KIGHOSTE INTERNATIONALT

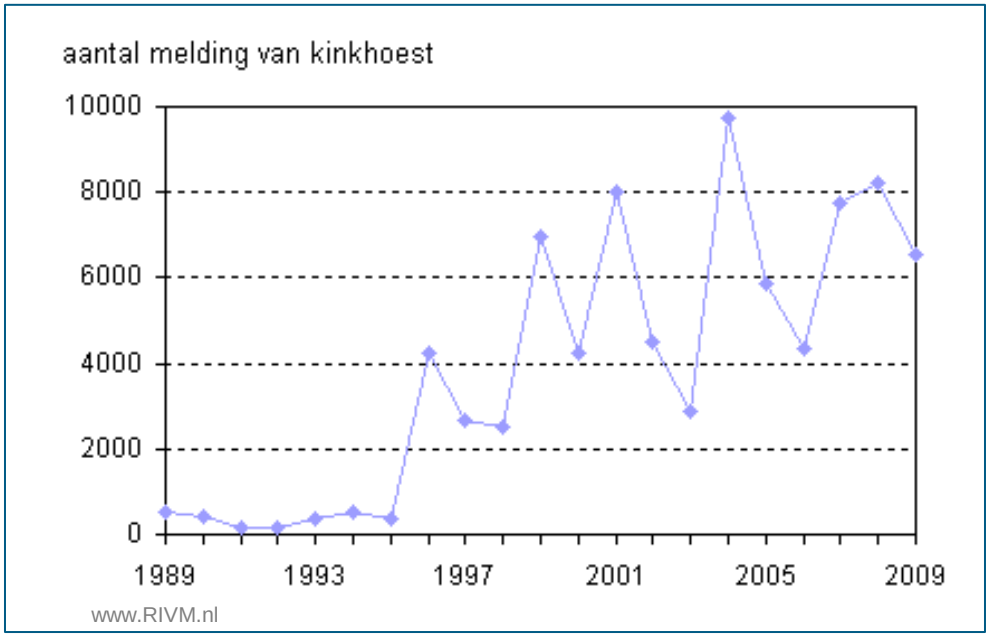
NASA

KIGHOSTE INTERNATIONALT

STATENS SERUM INSTITUT

- Mange lande har set en markant stigning i forekomsten af kighoste.

- Årsagen er ukendt men kan skyldes:
  - Bedre diagnostiske muligheder
  - Højere kendskab til kighoste i alle aldersgrupper
  - Højere kendskab til atypisk kighoste
  - Evolution af bakterien



KIGHOSTE INTERNATIONALT

STATENS SERUM INSTITUT

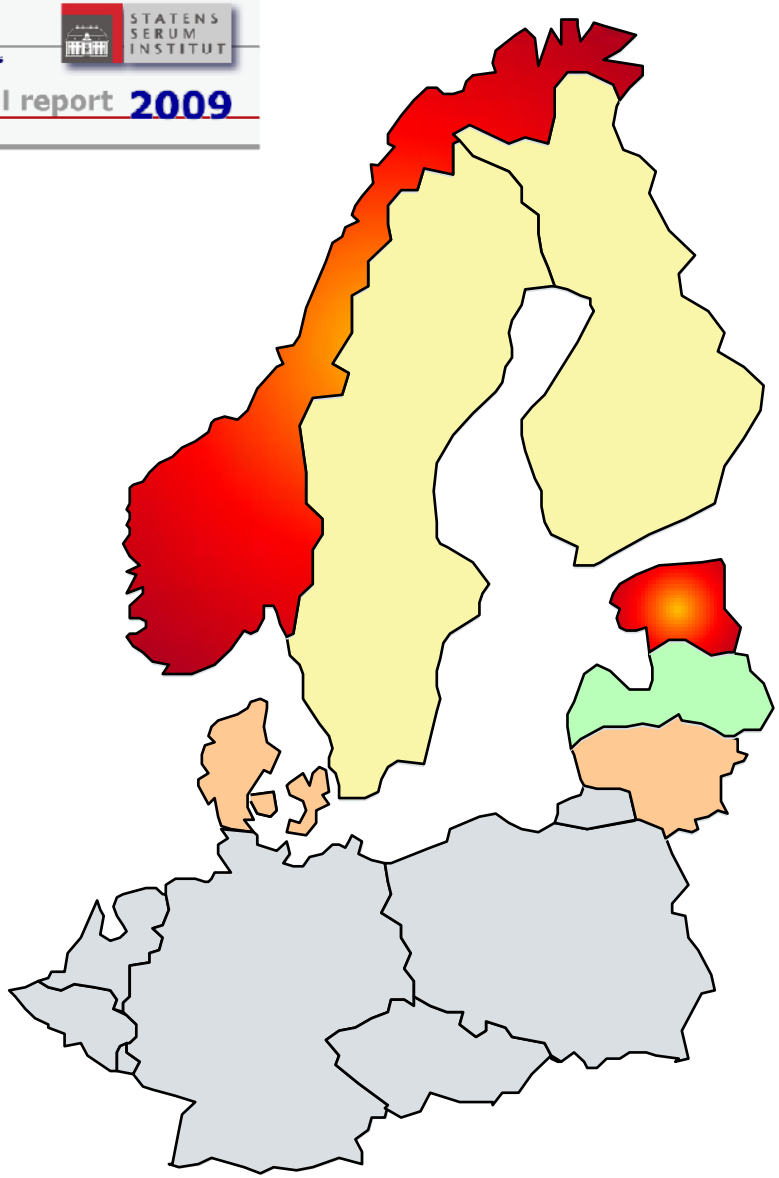
EUVAC.NET
A surveillance Community Network for Vaccine Preventable Infectious Diseases

STATENS SERUM INSTITUT

Pertussis surveillance annual report 2009

www.euvac.net

Land	Incidens 2009 pr. 10^5
Danmark	9,8
Sverige	3,0
Norge	114,3
Finland	5,0
Estland	46,9
Letland	0,4
Litauen	7,0



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Malta 2009: 0 tilfælde
INGEN DIAGNOSTIK

Forskelle i :

- Laboratorie-metoder
- Anmeldelses-system
- Diagnose-krav mht. antibiotika
- Økonomi for lægerne
- Viden blandt læger

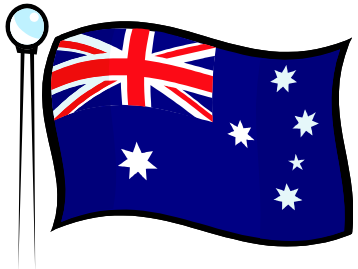
Viden blandt befolkningen

etc.

KIGHOSTE INTERNATIONALT

STATENS SERUM INSTITUT

- Mange lande har indført vaccination af voksne. Især for at undgå smitte til spædbørn.



ACT Health

ACT Health is providing free vaccine to parents and grandparents who have regular contact with infants less than 12 months of age. Partners and grandparents can also access this vaccine in the last month of pregnancy. The vaccine can be obtained via GPs or through hospital maternity units for new mothers until 30 June 2011.

New South Wales Department of Health

For a limited time, free whooping cough booster is available for new parents, grandparents and carers of babies under 12 months of age.

Northern Territory Department of Health and Families

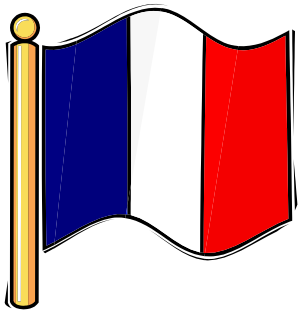
The pertussis vaccine is free to parents and close family members when administered within 7 months of the birth of a child.

http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/immunise-pertussis

KIGHOSTE INTERNATIONALT

STATENS SERUM INSTITUT

- Mange lande har indført vaccination af voksne. Især for at undgå smitte til spædbørn.



Recommandations particulières

La vaccination contre la coqueluche est également recommandée chez les adultes susceptibles de devenir parents dans les mois ou années à venir (**stratégie du cocooning**) ainsi que, à l'occasion d'une grossesse, la mise à jour des vaccinations pour les membres de l'entourage familial (enfant qui n'est pas à jour pour cette vaccination, adulte qui n'a pas reçu de vaccination contre la coqueluche au cours des dix dernières années), selon les modalités suivantes :

- durant la grossesse pour le père, la fratrie et, le cas échéant, l'adulte en charge de la garde du nourrisson[2] pendant ses 6 premiers mois de vie ;
- pour la mère en post-partum immédiat (l'allaitement ne constitue pas une contre-indication à la vaccination anticoquelucheuse).

Est également recommandé le rattrapage **des professionnels en contact avec des nourrissons trop jeunes pour avoir reçu trois doses de vaccin coquelucheux**:

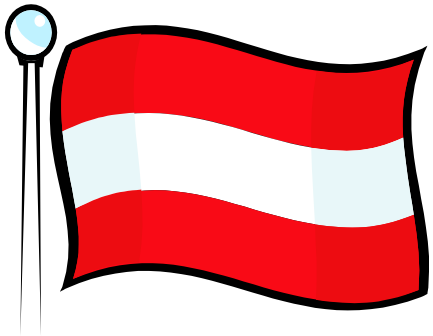
- personnel médical et paramédical des maternités, des services de néonatologie, de tout service de pédiatrie prenant en charge des nourrissons de moins de 6 mois,
- personnel chargé de la petite enfance.

http://www.sante.gouv.fr/IMG/pdf/Calendrier_vaccinal_-_Recommandations_2012.pdf

KIGHOSTE INTERNATIONALT

STATENS SERUM INSTITUT

- Mange lande har indført vaccination af voksne. Især for at undgå smitte til spædbørn.



Erwachsenenimpfung

Ab dem 19. Lebensjahr soll bis zum 60. Lebensjahr eine Auffrischungsimpfung mit Pertussis als Kombinationsimpfstoff mit Diphtherie (d), Tetanus (T), und ev. Polio (IPV) alle 10 Jahre und ab dem 60. Lebensjahr alle 5 Jahre erfolgen.

http://bmg.gv.at/cms/home/attachments/3/3/6/CH1100/CMS1327680589121/impfplan_2012_final,_1.2.2012.pdf

KIGHOSTE I FREMTIDEN

KIGHOSTE I FREMTIDEN

STATENS SERUM INSTITUT

- Vi vil se en stigning i kighoste i Danmark, primært på grund af den udvidede diagnostik og øget kendskab til kighoste blandt voksne

- Måske vil der blive introduceret kighostevaccination til kommende forældre samt til personer med kontakt til nyfødte og små børn

OPSUMMERING

STATENS SERUM INSTITUT

- Vaccination beskytter blot 5-10 år
- Tidligere episode af kighoste beskytter blot 5-10 år

- Antibiotika vil mindske smitten, men vil ikke hjælpe på symptomerne
- Der findes ingen bevist virksomme midler til at standse hosten

- Kighoste ses blandt alle aldersgrupper
- Kighoste hos voksne er den primære smittekilde til de små børn
- Kighoste kan forekomme atypisk uden kigen eller opkastninger

- Kighoste kan påvises ved både dyrkning, PCR og serologi
- Prøver til dyrkning og PCR skal være fra nasopharynx
- Voksne vil ofte søge læge sent, og da vil kun serologi kunne anvendes

That's all Folks!