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AN OVERVIEW OF PERTUSSIS REEMERGENCE AND EVIDENCE OF ITS RESURGENCE IN BRAZIL

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ABSTRACT

About two thousand cases of pertussis are reported in Brazil each year, with the highest incidence and mortality rates occurring in children under one year old. The disease is becoming common in Brazil; however the state of Rio de Janeiro has been showing low reporting figures in relation to other states in the Southeast region. This research work aimed to evaluate the difficulties faced by medical teams when confirming suspect cases of pertussis in healthcare units throughout the state of Rio de Janeiro and to use available data to confirm pertussis diagnosis within the last two years. Epidemiological surveys were conducted among medical personnel from healthcare units who presented the main obstacles to confirming suspect cases. Results show that a lack of laboratory diagnosis, poor differential diagnosis, low knowledge of the disease and a lack of clinical experience are, among other factors, relevant to the low reporting rates in the region.

KEY WORDS: Pertussis; reemerging disease; medical diagnosis; public health; Rio de Janeiro.

RESUMO

Um panorama da re-emergência de pertussis e a evidência de seu ressurgimento no Brasil

Cerca de dois mil casos de coqueluche são relatados no Brasil a cada ano. Crianças com menos de 1 ano de idade pertencem ao grupo com maiores taxas de incidência e letalidade. Apesar de a doença estar se tornando cada vez mais frequente no Brasil, o estado do Rio de Janeiro vem apresentando baixos índices de informação comparativamente a outros estados da Região Sudeste. Portanto, este trabalho teve como

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objetivo avaliar tanto as dificuldades enfrentadas pelas equipes médicas ao confirmar casos suspeitos de coqueluche em unidades de saúde em todo o estado do Rio de Janeiro quanto a disponibilidade de dados para confirmar o diagnóstico da coqueluche nos últimos dois anos. O levantamento epidemiológico foi realizado entre o pessoal médico de unidades de saúde que apresentaram dificuldades para a confirmação de casos suspeitos. Os resultados indicaram alguns fatores relevantes para as baixas taxas de notificação na região: falta de diagnóstico laboratorial, inconsistência do diagnóstico diferencial, escassez de conhecimento sobre a doença e falta de experiência clínica.

DESCRITORES: Coqueluche; doença reemergente; diagnóstico clínico; saúde pública; Rio de Janeiro.

INTRODUCTION

Pertussis reemergence is a widely studied and verified issue in developing countries. Analyses of factors that contribute to this resurgence phenomenon are complex since even in countries with extensive immunization coverage, the disease is still being reported. There have also been changes to its epidemiological profile, translating into an increase in disease incidence among teenagers and young adults, especially after the period between 1980 and 1990 (1, 7, 15).

Studies have demonstrated that France and the United States have been investing significantly in studies of the disease's fresh outbreak in the last 30 years. Such studies point to the following as determinant and relevant: quality of case reporting, clinical examination and laboratory testing; decreased immunization coverage; relative efficacy of vaccines; gradual loss of immunity (approximately 10 years after the last dose is administered); genetic changes to bacteria with natural selection of variants resistant to the vaccine and an increase in asymptomatic carriers. In developed countries, there may be other factors responsible for this reported resurgence of the disease, such as the use of new diagnostic methods and improved epidemiological surveillance systems (1, 3, 17-19).

We emphasize the possibility of a global dimension to this resurgence, with specific different factors and contexts in developed countries and in developing countries. We notice, above all, the vaccination scenario which has been historically different in terms of prevention policies adopted by countries. This shows that disease understanding and control are not well-grounded on the criterion of universal application of immunization, based on its absolute value. When the triple vaccine was adopted by countries that organized extensive vaccination strategies, it was believed that this resource would be able to promote efficient progressive control of the disease. However, in global terms we highlight that the reemergence of pertussis is a significantly relevant public health issue. Additionally, in poor countries pertussis is an important cause of child morbidity and mortality, aggravated by malnutrition and the incidence of bronchopneumonia.

Pertussis is potentially dangerous. It is an acute, highly contagious infectious disease transmitted by a bacterium initially called *Haemophilus pertussis* and later called *Bordetella pertussis* - from the Latin *per* (intense) and *tussis* (cough).

Contagion occurs by propagation of nasopharyngeal droplets when a sick individual coughs, sneezes and speaks. It requires close contact, less than 1 meter, such as in homes, work and study environments. Children are a frequent source of infection for adults and vice-versa. It should be noted that until 1940 it was the greatest cause of child mortality worldwide (3, 7, 12, 13).

Adults and teenagers can get infected and have the typical disease; others may remain oligosymptomatic and a significant group may develop an unapparent infection. Therefore, it has been considered one of the factors that influences the persistence of this disease in communities with extensive immunization coverage. In a study with 664 teenagers and adults who showed symptoms of the disease, Senzilet et al. (14) report that 77% of the surveyed group had been immunized for pertussis and 6.5% (22.8% in patients over 50 years old) categorically reported having had the disease when they were children.

The World Health Organization (WHO) estimates that in 2008 1.5 million children died of diseases that could have been prevented by routine immunization. This represents 17% of total mortality among children younger than 5 (5, 7, 18).

Although it is an immunopreventable disease, WHO revealed that in 2010 global occurrence of pertussis reached 91,689 cases, with over 195 thousand deaths; this represents 13% of immunopreventable diseases that affect children (7, 17, 19).

Epidemiological studies conducted in France in the 1990s showed increasing contagion among teenagers and adults and that the incidence of pertussis remained high in Europe: 12.2/100,000 inhabitants, although common sense has "vulgarized" pertussis as a children's disease. Further studies found that immunization coverage varied widely across Europe: According to data obtained at the time the incidence of pertussis was significant in France, Holland, Denmark and Great Britain. Germany had low immunization coverage and was reinitiating vaccination across the board in 1991; in Italy immunization was still very low. Great Britain experienced two epidemics (1978 & 1982) and since then it has resumed active vaccination. Sweden implemented an extensive vaccination program in the 1960s; this policy was suspended in 1979 over fears of side effects and because they verified the vaccine was relatively inefficient in that country. In Russia vaccination was inconsistent. In countries where coverage was extensive, such as France, the same resurgence was observed as in the United States, that is, incidence was significant among young adults. This favored the contamination of babies who had not been immunized at all or who had not been fully immunized. Studies found that in France and the USA pertussis peak distributions according to age were in opposite extremes, that is, before 6 months or after 20 years of age, indicating the need for a new epidemiological outlook on the disease (7, 9, 17-19).

A report about pertussis' profile in the United States between 1997 and 2000 summarized that the increase in this disease in the 1980s continued throughout the 1990s. Compared with data from 1994-1996, the disease's incidence rate increased among teenagers and adults, 62% and 60% respectively; and among children younger

than 1 it increased by 11%. However, incidence fell by 8% among children aged 1 to 4 and remained stable among children aged 5-9. Such increases may reflect a change in disease reporting or real increase in incidence. In 1995 the criterion for reporting pertussis changed in two ways: use of PCR as a method for diagnostic confirmation and more detailed collection of data about disease occurrence, which provided for more precise epidemiological analyses. Despite vaccination effectiveness, pertussis still occurs in the United States across all age groups. The disease remains more significant among children younger than 1, who also have higher complication and death rates. Considering there are still high vaccination rates among pre-school children, prevention efforts should focus on treating pertussis cases in order to prevent greater disease communication, by using antimicrobial prophylaxis in cases of contacts aiming to minimize the exposure of children younger than 1 to older children and adults with "cough diseases" (3, 8, 9, 10, 17).

Still regarding the North American reality, more recent data confirm the aggravation of pertussis, which shows a new epidemiological pattern. Between 2004 and 2005 there was "a boom of this disease in the United States with 25,827 cases. In those two years case reporting for people aged 10 to 19 years old grew 15.6 fold in relation to 1990. Among individuals older than 20, this increase was 16.7 higher. In 2008 the disease receded, but even so it infected 13,278 people. Approximately half of infected individuals were teenagers and adults. Incidence among children between five and nine years old increased significantly, totaling 20% of reported cases, as opposed to 13% in 2007 and 10% in 2006. In 2010, according to the Centers for Disease Control and Prevention of the North American government (DCD), the number of cases increased significantly in several regions. In California, where over two thousand cases and eight deaths among babies were recorded, incidence increased over seven times in relation to the same period in 2000 (5, 17, 18, 19). Relevant information about the disease's profile in Latin America showing its reemergence is being published by publications targeting practicing medical professionals, especially in the field of pediatrics. The Correo da Sociedad Argentina de Pediatria (6) states that "in Argentina the epidemiological surveillance system has detected in the second semester of 2003 an increase in the incidence of pertussis in several parts of the country, especially in the south of the Buenos Aires province, in Corrientes, Entre Rios and Formosa; children affected the most were those under a year old and secondly the group aged 2-4" (6, 9, 18).

A study about changes in Chile's epidemiological profile used information processed by the Expanded Immunization Program (PAI) managed by its Ministry of Health and found out that the only disease detected by the Program which recorded significant increase in the 1990s decade was pertussis (59 cases in 1990, 361 in 1995 and 3,551 in 2000) (8, 10, 11).

Trevizan and Coutinho (16) used 2002 data from the Ministry of Health about the prevention and control situation of transmissible diseases in Brazil to state that throughout that period an average of 2 thousand annual pertussis cases had

been reported. Higher lethality was found among children younger than one year old and this incidence was even higher among children younger than six months. In summary, the general picture shows an increase in pertussis cases in global terms and, according to Bricks et al. (4), "in the last five years 'whooping cough' cases have tripled in Latin America, according to a WHO and UNICEF report. In the state of São Paulo alone, the number of confirmed cases rose by 33% between 2006 and 2009. In 2006 there were 96 confirmed cases, as opposed to 128 in 2009" (3, 6-8, 12, 16, 17).

After the implementation of the National Immunization Program (PNI) in 1983 the disease rate decreased throughout the country, especially due to extensive immunization coverage for all three doses (10, 15).

However, even with average coverage of 95% in all municipalities, the incidence of this disease has been increasing in some Brazilian states (10, 15).

In Brazil there are no studies that allow answering beyond a reasonable doubt whether pertussis is reemerging or not, especially considering the country's continental size as well as socioeconomic, climate, cultural and infrastructure variations concerning the access to the public healthcare system and disease reporting systems. Such are relevant aspects of the Brazilian reality that affect results of analyses about the disease's epidemiological profile. However, a few hypotheses may be suggested. One of them is related to the possibility that the disease is indeed imperceptibly reemerging in Brazil, although in the last few years a few states have reported significant increases in the number of cases (6, 10, 15, 16).

In the North region, the states of Amazonas and Pará showed rates above 70 reported cases (10, 15).

In the Middle West region the Federal District has been showing a progressive increase in case reports in relation to the other states, even when compared with the state of Goiás, which reported over 70 cases in 2004 (7, 10, 15).

In the Northeast region, in 2012 the state of Pernambuco showed an increase in the rate of notification compared to the year 2011, with 250 cases in 2012 and 77 cases in 2011. However, the state of Bahia drew attention to the significant increase in notifications in the past two years, 147 cases in 2012 and 166 cases in 2011 compared with 17 cases reported in 2010. Rio Grande do Norte also showed considerable increase in the rate of disease cases, 134 notifications in 2012, 60 in 2011 and 14 in 2010 (10, 15).

In the South region, Rio Grande do Sul has recorded more regular rates, always above 100 cases in the period from 2004 to 2009, higher than the other states in the same region, however, in the past two years, notifications increased from 147 cases in 2011 to 813 cases in 2012. Other states also showed an increase in reports in the year 2012. The state of Santa Catarina showed 265 cases reported in 2012, much higher than the 48 cases in 2011. The State of Paraná has shifted to 391 cases in 2012 compared to 148 cases in 2011 (10, 15).

In the Southeast region, the state of São Paulo showed a considerable rate increase from 2010 to 2012. 156 cases were reported in 2010, 854 in 2011 and 1,057

in 2012. The state of Rio de Janeiro, in the same period presented 254 case reports in 2012 compared to 99 cases in 2011 and 18 in 2010 (Table 1) (10, 12, 15).

Table 1. Pertusis in the State of Rio de Janeiro.

Counties	2012	2011	2010	Counties	2012	2011	2010
Angra dos Reis	5	-	-	Nilópolis	1	-	-
Araruama	1	-	-	Niterói	20	1	-
Bom Jesus do Itabapoana	2	-	-	Nova Friburgo	8	1	-
Cachoeiras de Macacu	7	-	-	Petrópolis	1	3	-
Campos dos Goytacases	7	8	1	Rio de Janeiro	127	79	16
Duque de Caxias	20	4	1	São Fidelis	1		
Itaboraí	10	2	-	São Francisco Itabapoana	2	-	-
Itaocara	1	-	-	São Gonçalo	13	-	-
Itaperuna	3	1	-	São João da Barra	1	-	-
Itatiaia	1	-	-	Três Rios	4	-	-
Macaé	11	-	-	Varre-Sai	1	-	-
Magé	1	-	-	Vassouras	1	-	-
Natividade	5	-	-	Total	254	99	18

This study aims to determine the main difficulties faced by healthcare professionals when diagnosing reemerging diseases, especially pertussis.

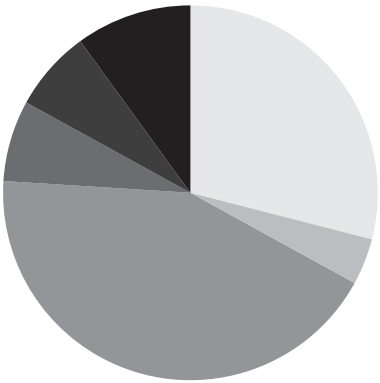
METHODOLOGY

We carried out qualitative research by conducting a survey which involved physicians from several healthcare units, three of them public and two military, in the state of Rio de Janeiro in 2010 and 2012, all operating in the following areas: outpatient care, pediatrics, infectology and pulmonology. 185 physicians participated in the epidemiological investigation, from medical residents to professionals with more than ten years of clinical experience, in five health units. The information was collected through interviews and applications of questionnaires regarding the resurgence of pertussis in Brazil.

RESULTS

The medical team that took part in this research was made of residents (15%), physicians with 1-5 years of clinical experience (29%), physicians with 6-10 years of clinical experience (29%), physicians with over 10 years of clinical experience (39%), and physicians who did not provide that information (5%). This medical team covered several specialties, from general practitioners (41%), to infectologists (24%), pediatricians (21%), pneumologists (7%) and others who did not inform their specialty (7%).

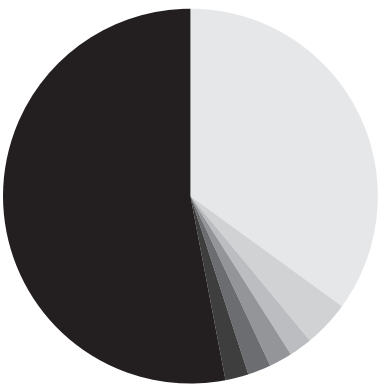
We identified 43% of patients who received care in studied healthcare units in the last two years showing the classic clinical profile of the disease. Although the number of patients who received care ranged from 1 to 10, 10% of those units had 30 patients or more (Graph 1).



No case	29%
Not informed	4%
1 to 10	43%
11 to 20	7%
21 to 30	7%
31 to 40	10%

Graph 1. Average number of patients with a clinical profile including coughs > 14 days associated with uncontrollable coughing, paroxysm, 'whooping' or post-cough vomiting in the last 2 years.

Based on information about the number of patients with pertussis in the same period, we verified that only 53% of professionals reported not having treated any suspected cases of the disease; 35% reported 1-5 cases diagnosed within that period; 4% reported 6-10 treated cases; and 6% reported treating over 11 cases (Graph 2).

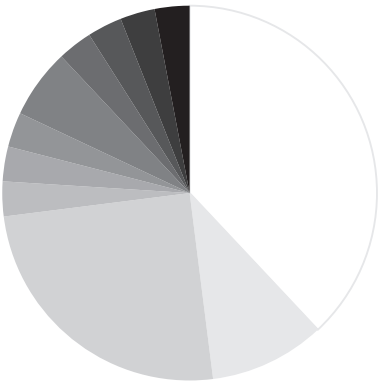


1 a 5	35%
6 a 10	4%
11 a 15	2%
16 a 20	2%
> 20	2%
Uninformed	2%
No case	53%

Graph 2. What is your estimate of the routine patient with suspected pertussis in recente years?

In cases where patients were confirmed to have pertussis, we analyzed the procedure adopted by healthcare units to avoid disease communication to other patients: 38% reported that patients with suspected pertussis are isolated in rooms with air flow filtering systems; 28% isolated patients in rooms with no air flow filtering system; 16% did not isolate patients; 14% did not provide that information; 8% reported that their healthcare unit does not isolate patients; and 1% isolate patients in infirmaries.

Regarding the last diagnosis of the disease in their clinical routine, 38% were unable to provide information; 25% stated there had been no suspected cases; and 27% informed us they had diagnosed patients some time ago, that is, over weeks, months or years (Graph 3).



	Unable to provide information	38%
	Did not answer	10%
	No suspected cases occurred	25%
	5 years ago	3%
	4 years ago	3%
	1 year ago	3%
	2 years ago	6%
	2 months ago	3%
	6 months ago	3%
	1 week ago	3%
	19 year ago	3%

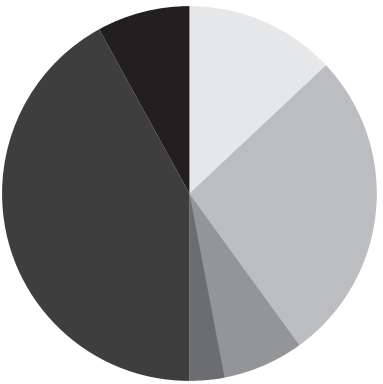
Graph 3. When did you last diagnose a patient with pertussis in your clinical practice?

It should be noted that the greatest hurdle pointed out by physicians when making a diagnosis is lack of access to laboratory diagnosis as the main technique to confirm the disease (42%). Other factors were pointed out as equally important, such as assessing the patient's clinical profile more precisely and interpreting symptoms correctly, which is not always accomplished (Graph 4).

The association between age group, greater clinical knowledge about the disease and performing laboratory tests to confirm pertussis in its initial stages were all pointed out as relevant factors for precise diagnosis.

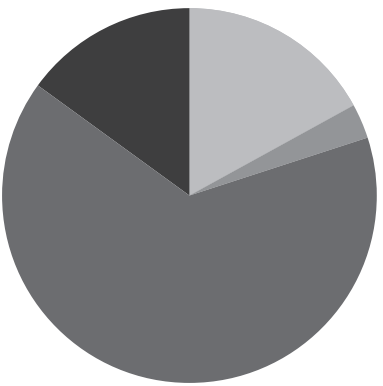
Graph 5 shows the percentage of answers about difficulties found when making a diagnosis and clinical experience regarding reemerging and/or neglected diseases provided during professional training, that is, during medical residency. 65% of professionals stated that current residency programs lack that experience.

Such results also demonstrate that it is necessary to place greater emphasis on the issue of reemerging and neglected diseases during academic education, since the interviewed professionals are all doctors who have completed their education, as reported before, from those in their residency (15%) to those with over ten years of clinical experience (39%).



Greater Knowledge about the disease	13%
Difficulties interpreting symptoms	27%
Difficulty diagnosing adults	8%
Lack of training to health care professionals	2%
Lack of laboratory diagnosis	42%
Did not answer	8%

Graph 4. In your opinion, what are the greatest difficulties currently encountered for making a final diagnosis of a patient with suspected pertussis.



Yes	17%
Sometimes	3%
No	65%
Did not answer	15%

Graph 5. In your perception, does the current medical residency program provide training regarding clinical features of remerging and/or neglected diseases?

Regarding the continuing education program, 33% of respondents declared there is no such program in their healthcare unit; 14% reported it has not been implemented; and 36% reported that there is occasional professional training.

DISCUSSION AND CONCLUSION

This study demonstrates that pertussis is under-reported in Rio de Janeiro, particularly due to the lack of training provided to healthcare professionals to recognize the disease's clinical symptoms. This results in incorrect diagnosis, often due to lack of infrastructure for performing laboratory tests for confirmation.

Brazil lacks studies about the reemergence of pertussis which take into account all aspects related to our national reality that might interfere with analyses about the epidemiological behavior of the disease, including the possibility that the disease is indeed imperceptibly reemerging in Brazil, aggravated by the fact that currently it can no longer be considered an exclusively pediatric disease. It requires greater recognition from physicians and complex actions regarding diagnosis, surveillance, disease control and other specialties that are within the realm of public health so that, if necessary, people are ready to realign their action strategies.

There is need to develop new research methodologies that address diagnosis, allowing rapid confirmation of the disease as a strategic action in controlling the resurgence of the pathology. According to Ferronato et al. (8) a study in a health facility in the State of São Paulo found the incidence of hospitalized infants with respiratory viral infections, suspected of pertussis, among the 67 patients analyzed at this health facilities, only 44% were positive for pertussis, 26% were positive for respiratory viruses, 35% etiological agents not identified and 5% was co-detection for pertussis and respiratory viruses. This demonstrates the need for improvement in confirmation of pertussis in its early stages.

Health professionals should be trained in diagnosing the re-emerging diseases, especially emergency care professionals who have contact with suspected or confirmed pertussis patients, adopting biosafety protocols to prevent the spread of disease in their health unit. Pascual et al. (11) described an outbreak of pertussis among healthcare workers. The case occurred in professionals on duty in an operating theatre, exposing patients and relatives. Twelve of the health professionals who did not adopt biosafety procedures, such as use of safety masks, presented clinical pertussis.

The possibility of resurgence of pertussis in Brazil has already been highlighted in several studies in the literature, according to Druzian et al. (7) the incidence of pertussis in the midwestern region of Brazil in the period from January 1999 to December 2008, registered in the Ministry of Health was 561 suspected cases, 238 (42.4%) of which were confirmed, especially in children less than six months (61.8%) and with incomplete immunization (56.3%).

Due to this, it is possible to notice a higher incidence of the disease in the group that had not finished its primary immunization (three doses plus a booster dose), and also draw attention to the need for studies for inclusion in the National Immunization Program, vaccinating pregnant women, thereby protecting children under two months old, preventing the disease from spreading in the age range that has not been immunized.

With this challenge ahead, we believe that it is crucial to implement training programs about remerging diseases, especially pertussis, targeting the daily work of healthcare professionals, considering the need to clarify diagnosis, treatment and also isolation of patients who have this disease. As our study also showed, patients are often wrongly isolated from others or even when they return to their homes.

The main limitations encountered during the preparation of this study were based on the following factors: the public health units who participated in this research were chosen randomly, considering their location, the profile of clinical care and the existence of emergency care for adults and children. The health unit medical team of pediatrics, infectious diseases, pulmonology and general practice (185 physicians) surveyed, were chosen randomly.

Other limiting factors were: difficulty pointed out by doctors in the diagnosis of reemerging diseases, consequently increasing under-reporting.

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