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MINIREVIEWS

Epidemiology and Clinical Spectrum of Brazilian Purpuric Fever

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INTRODUCTION

This paper is divided into four sections. The first provides a historical perspective of *Haemophilus aegyptius*, an organism that was previously, before the first description of Brazilian purpuric fever (BPF), known to cause only noninvasive infections. The second section reviews the brief history of BPF since the first recognized outbreaks in 1984, and the third describes epidemiologic and clinical aspects of BPF. The last section reviews the most recent cases of BPF in Brazil and describes surveillance for conjunctivitis and BPF in São Paulo State, Brazil, the area with the most known cases of BPF. Information presented at the Brazilian Purpuric Fever Workshop held at the Centers for Disease Control, Atlanta, Ga., on 13 and 14 May 1988 was abstracted for this review.

HISTORICAL VIEWS OF *H. AEGYPTIUS*

H. aegyptius, the etiologic agent of BPF (5, 12, 17), has long been known as a cause of seasonal epidemics of acute purulent conjunctivitis. Acute purulent conjunctivitis is an age-old disease, often referred to as pink eye or gnat sore-eye, that continues to occur in parts of the world with hot climate and high incidences of gnats and/or flies. Wilson (34) cites a 1583 paper that reported that epidemics in Egypt occurred at the time of the khamsin, the hot Sahara wind that occurs before the vernal equinox. The causative organism was first observed by Koch in 1883 (19) when, during activities of the German Cholera Commission in Egypt, he studied 50 patients suffering from Egyptian eye disease. He found two types of conjunctivitis, the more serious of which was caused by a "gonococcus-like organism." As for the more benign form, Koch wrote, "In the less dangerous process very small bacilli are regularly found in the pus," referring to what was later identified as *H. aegyptius*.

Three years later in his classic paper (31) and subsequent publications (32, 33; J. E. Weeks, Trans. 10th Int. Med. Congr., abstr. no. 10, p. 38, 1890), Weeks described the essential characteristics of *H. aegyptius*: its high contagiousness, direct transmission from patients to volunteers, pathogenesis, pathology, treatment, and epidemiology. Of historical interest is Weeks' observation that *H. aegyptius* grew on agar medium only in the presence of an associated club-like organism (*Corynebacterium xerosis*), probably the first observation of the *Haemophilus* satellite phenomenon.

Weeks reported outbreaks of acute conjunctivitis in the summer and fall in New York City and surrounding areas, as well as in southern New England. The disease was highly contagious; Weeks described yearly epidemics at the New York Infant Asylum, clustering of conjunctivitis in families (32), and epidemics in boarding schools (33). Although all ages were affected, illness occurred most frequently in infants and young children. The duration of infection with therapy was usually about 2 to 3 weeks (33); corneal damage was not reported. He also commented that the disease was probably worldwide in distribution and reported knowledge of acute conjunctivitis in Egypt, France, and England. In 1941, Monteiro Salles (22) reported a large epidemic of *H. aegyptius* conjunctivitis in Campinas, São Paulo State, Brazil.

Since Weeks' papers, reports of *H. aegyptius* conjunctivitis in the United States have been limited to the southern states. Bengtson (2) studied the disease in southern Georgia in 1931 and 1932 and observed that acute conjunctivitis occurred during the high breeding season of the eye gnat, *Hippelates pusio*. She cited reports of the same observation in the Coachella Valley of California, other areas of the southern United States, and other parts of the world. She suggested that the gnat, attracted to eye secretion, is a mechanical transmitter and that within families and schools the highly contagious disease is transmitted from person to person. Acute conjunctivitis has continued to be a health problem in the southern states; Davis and Pittman (14) studied it in the lower Rio Grande valley, and Davis and Hines (13) and also Buehler et al. (8) studied it in Georgia. Davis and Pittman observed gnat transmission of *H. aegyptius* to a culture plate on which a gnat taken from the eye of

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a baby with conjunctivitis was permitted to walk (M. Pittman, unpublished data).

The Koch-Weeks bacillus has had many names (26), although neither Koch nor Weeks proposed one. Trevisan in 1889 (30) listed it as "*Bacillus aegyptius*" in the first classification treatise designating bacteria by Latin binomial names. Trevisan's treatise was unknown in the United States when the first edition of *Bergey's Manual of Determinative Bacteriology* was published in 1923 (3) with the name "*Hemophilus conjunctivitidis*" (Kruse). *H. aegyptius* was first used in the seventh edition of *Bergey's Manual* (6) after Pittman and Davis (26) had described certain differential characteristics between this organism and *H. influenzae*. After a study of the names of the species of all known bacteria, the Judicial Commission of the International Committee on Systematic Bacteriology issued the approved lists of bacterial names in 1980 (28), in which the Koch-Weeks bacillus was listed as *H. aegyptius*; this name was also used in *Bergey's Manual of Systematic Bacteriology* in 1984 (16).

After Pfeiffer discovered *H. influenzae* in 1892 (24, 25), some confusion arose about whether *H. aegyptius* was different from *H. influenzae*; opinions prevailed, however, that radical differences existed between the two bacilli and that *H. aegyptius* was the cause of acute conjunctivitis (15, 23).

With the introduction of phenotypic and later phylogenetic techniques, the separation of the two organisms has been questioned. Although certain phenotypic characteristics have been useful for differentiating *H. aegyptius* from *H. influenzae* (18, 20), recent studies have shown that no one test serves to differentiate the two organisms (10, 20). DNA hybridization studies (1, 7, 11, 27) indicate that *H. influenzae* and *H. aegyptius* are phylogenetically one species.

Referring to both organisms as *H. influenzae*, however, does not account for the propensity of *H. aegyptius* to cause a primary, localized, highly contagious conjunctivitis that occurs seasonally and epidemically in hot climates (2, 26). To account for the fact that the two organisms cannot be separated phylogenetically but appear to differ clinically, the name *H. influenzae* biogroup aegyptius has been used instead of *H. aegyptius* (7).

After being studied for more than a century, an organism previously associated only with benign conjunctivitis has been shown to cause a highly fatal illness, BPF.

HISTORICAL REVIEW OF BPF

During October through December 1984, 10 children in the town of Promissao (population, 20,430) in São Paulo State, Brazil, developed a severe illness characterized by high fever, abdominal pain and vomiting, hemorrhagic skin lesions, vascular collapse, and death (4). Although the illness was clinically similar to meningococcemia, two distinct features were noted: the absence of meningitis in all of the children and a statistical association between illness and a recent history of conjunctivitis; the disease was named BPF. *H. influenzae* biogroup aegyptius was isolated both from a nonaseptically obtained scraping of a petechia of a child with BPF and from children with conjunctivitis but not BPF in the same town. Laboratory studies demonstrated that *H. influenzae* biogroup aegyptius with a particular plasmid was epidemiologically associated with BPF (G. M. Carlone, F. O. Sottnek, L. W. Mayer, K. A. Birkness, and the BPF Study Group, Abstr. Annu. Meet. Am. Soc. Microbiol. 1986, C-5, p. 328).

During the epidemiologic investigation of the Promissão outbreak, investigators became aware of a similar outbreak consisting of 13 cases and seven deaths in the city of Londrina (4), 250 km from Promissão in the neighboring state of Paraná. A working case definition based on the clinical characteristics of these epidemic cases was developed (4). Additional sporadic cases were identified in Promissão, Londrina, and six other towns near Promissão.

In 1986, the etiology of BPF became clear when a third outbreak occurred in Serrana, a small town in northeast São Paulo State (5, 17). *H. influenzae* biogroup aegyptius was isolated from normally sterile body fluids (nine times from blood and once from cerebrospinal fluid [CSF] contaminated with blood) during an outbreak of BPF. An additional case was identified in Serrana that fit the previously established clinical case definition; two additional blood culture-positive and two CSF culture-positive sporadic cases were identified in four other small towns in the state. These data confirmed that *H. influenzae* biogroup aegyptius had a direct role in the pathogenesis of BPF. Subsequent studies have shown that a single *H. influenzae* biogroup aegyptius clone, hereafter called the BPF clone, is responsible for all Brazilian cases of BPF.

The previously developed clinical case definition was revised as follows to reflect the knowledge that BPF is due to *H. influenzae* biogroup aegyptius bacteremia: (i) febrile illness in a child with isolation of *H. influenzae* biogroup aegyptius from a normally sterile body site (e.g., blood or CSF) or (ii) acute illness in a child 3 months to 10 years old characterized by a fever of 38.5°C (101.3°F) or higher, abdominal pain and/or vomiting, development of petechiae or purpura, and no evidence of meningitis; a history of conjunctivitis within the 30 days preceding the onset of fever; absence of *Neisseria meningitidis* as determined by blood cultures taken before antibiotic administration or serum or urine antigen detection. If obtained, other laboratory tests should be negative, including CSF with 100 or fewer leukocytes per μl, and negative by culture or antigen detection for pathogenic bacteria other than *H. influenzae* biogroup aegyptius; blood cultures negative for known pathogenic bacteria other than *H. influenzae* biogroup aegyptius; and serologic studies negative for known pathogens other than *H. influenzae* biogroup aegyptius. This case definition was developed and is still used for epidemiologic studies of BPF; it is not recommended for use to decide on therapy for individual patients.

Recently, a child with BPF was reported in Australia (21); the *H. influenzae* biogroup aegyptius isolated from this child is discussed elsewhere (9, 29). Although the symptoms of this child fit the clinical case definition of BPF, this case could simply represent a sporadic case of purpura fulminans associated with unencapsulated *H. influenzae* bacteremia. Thus, it is not clear whether the microbiologic data from this blood isolate will aid us in understanding the virulence mechanisms present in the BPF clone.

Several *H. influenzae* biotype aegyptius isolates from Pradópolis, São Paulo State, Brazil, are discussed elsewhere (9, 29). These conjunctival isolates are from individuals with conjunctivitis in a town where suspected BPF occurred. The suspected BPF was in a young child with a temperature of 40°C, vomiting, questionable perioral petechiae, and a history of conjunctivitis 15 days before the onset of fever. Blood cultures reportedly taken before administration of antibiotics were negative. These isolates are of considerable microbiologic interest, because they too are different from the BPF clone. However, because this strain has never been isolated from a sterile site of a patient with BPF, the epidemiologic significance of these isolates is not clear.

TABLE 1. Association of BPF with preceding conjunctivitis

Town	No. of patients with BPF with conjunctivitis/total with BPF (%)	No. of controls with conjunctivitis/ total no. (%)	*P* value	Mean (range) interval (days)[a]
Promissão	18/20 (90)	9/20 (45)	0.006	7 (1–45)
Londrina	13/15 (87)	1/8 (12)	0.0001	
Serrana	10/11 (91)	6/20 (30)	0.002	16 (1–60)

[a] Interval between onset of conjunctivitis and onset of fever in patients with BPF.

These caveats should be kept in mind when interpreting the microbiologic data from both the Australian and Pradópolis isolates.

EPIDEMIOLOGY AND CLINICAL PRESENTATION

The median age of the patients with BPF was 30 months in Promissão and 36 months in both Londrina and Serrana; all of the patients were ≤10 years old (4, 5). The outbreak in Promissão occurred in October through December 1984, the Londrina outbreak occurred in February through July 1984, and the Serrana outbreak occurred in March through June 1986. Recent clusters of BPF have occurred from December 1987 through February 1988. Although the data are limited, it appears that BPF occurs with the onset of warmer temperatures and is less likely to occur during the Brazilian winter.

Although BPF has occurred throughout Sao Pãulo State, it has been more common in small agricultural towns, despite the presence of many large industrial cities within the state. Londrina, in the state of Paraná, is the only city outside of São Paulo State known to have had BPF cases. São Paulo, however, is one of the most developed states in Brazil; it is unknown whether BPF occurs in other less developed areas of Brazil, where cases might not be recognized and diagnosed.

About 90% of patients with BPF give a history of conjunctivitis (Table 1) (4, 5). Case control studies in the three outbreaks studied all showed a significant association between conjunctivitis and BPF. In the Londrina study, controls were patients with culture-confirmed meningococcal disease, indicating that this finding was not due to recall bias in parents of children with a serious illness (4). The high percentages of controls with conjunctivitis in Promissão (45%) and Serrana (30%) emphasize the epidemic nature of conjunctivitis in towns with BPF outbreaks.

The mean interval between the onset of conjunctivitis and the onset of fever in BPF is 7 to 16 days, with a range of 1 to 60 days (Table 1) (4, 5). The conjunctivitis often resolves clinically before the onset of BPF.

Several case control studies have been done to identify risk factors for BPF. Use of insecticides, distance from the house of residence to sugar cane fields, socioeconomic variables, and exposure of children to a patient with the disease have not been associated with BPF (4, 5). A small case control study in Serrana suggested that day care attendance is a risk factor for BPF (matched odds ratio = 7; P = 0.08) (5). Although this finding must be confirmed, it is likely that day care offers a setting for transmission of *H. influenzae* biogroup aegyptius conjunctivitis.

Clinical presentation. Before it was known that BPF could be diagnosed by blood culture, the ability to define the clinical spectrum of BPF was limited to children with severe illness, although a broader range of illness was suspected (4).

TABLE 2. Summary of clinical laboratory evaluations of children with BPF in Brazil in 1984 and 1985

Laboratory test	No. of patients with BPF tested	Mean; median (range)
CSF		
Leukocytes (per μl)	22	26; 19 (1–57)
Polymorphonuclear leukocytes (no.)	18	6; 5 (0–19)
Lymphocytes (no.)	18	18; 19 (2–38)
Glucose (mg/dl)	21	54; 56 (21–108)
Protein (mg/dl)	22	28; 28 (12–61)
Blood		
Hemoglobin (mg/dl)	7	11.1; 11.4 (9.1–12.7)
Hematocrit (%)	17	35.9; 35.8 (29.0–48.0)
Leukocytes (10^3/μl)	19	13.2; 12.0 (3.5–34.0)
Bands (%)	14	14; 13 (2–32)
Polymorphonuclear leukocytes (%)	16	56; 55 (21–90)
Lymphocytes (%)	12	29; 31 (1–57)
Platelets (10^3/μl)	14	77; 50 (12–247)
Fibrinogen (mg/dl)	10	312 ; 310 (30–573)
Prothrombin time (s)	11	36; 27 (16–98)
Protein in serum (g/dl)	9	5.6; 6.4 (2.2–7.3)

The use of blood cultures in Serrana to identify cases has provided an expanded picture of the clinical spectrum of BPF in a few patients (5). Of the 10 children with *H. influenzae* biogroup aegyptius isolated from sterile sites, only half met the original case definition. The five children who did not meet this definition had illnesses that ranged from mild fever alone to fever with toxic, systemic symptoms and a rash without petechiae. The overall patient fatality rate since BPF was first recognized is about 70%.

Laboratory findings. Other than blood cultures, clinical laboratory findings in BPF are nonspecific (Table 2) (4). Leukocyte counts are often elevated (mean, 13,200/μl; range, 3,500 to 34,000/μl), with a preponderance of bands and polymorphonuclear cells. Thrombocytopenia (mean, 77,000/μl; range, 12,000 to 247,000/μl) and prolonged prothrombin time (mean, 36 s; range, 16 to 98 s) are also seen. Examination of CSF reveals a small number of leukocytes (mean, 26/μl; range, 1 to 57/μl), which are predominately lymphocytes. High levels of endotoxin have been found in sera of patients with BPF (4).

Diagnosis. The most specific test for diagnosing BPF is blood culture, which appears to be sensitive in severe cases, since five of six patients who fit the clinical case definition in Serrana had blood cultures positive for *H. influenzae* biogroup aegyptius (5). The organism is easy to isolate on standard media; however, routine blind subcultures must be performed, since the organism often does not cause turbidity of liquid media. In addition, blood culture bottles are not used in many areas of the state, and many children receive over-the-counter antibiotics before reaching the hospital, making in less likely that *H. influenzae* biogroup aegyptius will be isolated if present.

In the absence of positive blood cultures, an outbreak of BPF can be identified on the basis of a cluster of cases that fit the clinical case definition (i.e., are similar to meningococcemia). Isolation of the BPF clone from patients who currently have conjunctivitis or their contacts supports the diagnosis. Identification of sporadic cases is more difficult. BPF should be suspected in patients with illnesses that meet

TABLE 3. Definite and possible cases of BPF in 1987 and 1988

City	Date of 1st case	Population <10 yr old	No. of cases[a]			Rate[b]	Supporting evidence
			Definite	Possible	Total		
Nova Granada	12/4/87	2,511	0	2	2	80	BPF clone isolated from brother
Serra Azul	12/7/87	1,182	1	3	4	388	BPF clone isolated from blood
Serrana	12/12/87	4,492	1	0	1	22	Fits clinical case definition
Votuporanga	1/5/88	13,764	0	4	4	29	Agglutination-positive strain isolated from sister

[a] Definite, Fits case definition (*H. influenzae* biogroup aegyptius from sterile site or clinical case definition); possible, fever, hemorrhagic skin lesions, and recent history of conjunctivitis.

[b] Number of cases per 100,000 population <10 years old. The overall rate was 50.

the BPF case definition; supporting evidence can be obtained by isolating the BPF clone from case contacts.

Treatment. The appropriate treatment of conjunctivitis due to the BPF clone is problematic, since topical antimicrobial therapy does not prevent BPF, even if the conjunctivitis resolves clinically (5). *H. influenzae* biogroup aegyptius has been isolated from the conjunctivae and oropharynges of several BPF patients with topically treated, clinically resolved conjunctivitis, suggesting that asymptomatic carriage of the organism occurs despite topical therapy. A systemic antibiotic, such as rifampin, may be required for treating *H. influenzae* biogroup aegyptius conjunctivitis during BPF outbreaks. The efficacy of such therapy should be studied before it is used; furthermore, methods must be available locally to identify the BPF clone, since routine use of rifampin for all sporadic cases of conjunctivitis would be inappropriate because of the expense and potential development of resistance.

All isolates of the BPF clone are susceptible to both ampicillin and chloramphenicol, making this an appropriate parenteral combination for BPF (7). Although there have been no controlled therapeutic trials, some evidence suggests that early systemic antimicrobial therapy may improve the outcome (5). Other antibiotics to which the BPF clone is susceptible are amoxicillin-clavulanic acid, cefamandole, cefuroxime, cefotaxime, tetracycline, ceftriaxone, and rifampin (7). Most isolates of the BPF clone are relatively resistant to sulfamethoxazole-trimethoprim (MIC, 9.5/0.5 to 76/4 μg/ml) (7).

SURVEILLANCE FOR BPF AND CONJUNCTIVITIS IN SÃO PAULO STATE

São Paulo is a large state with a population of about 31 million, 16 million of whom live in greater São Paulo, the state capital. The Epidemiology Surveillance Center is responsible for statewide surveillance for infectious diseases. The state is divided into 62 regional health districts, 15 of which are in greater São Paulo. There are 1,032 health centers, the basic units that provide health care in the state. Laboratory support comes from 1 central and 15 regional Adolfo Lutz laboratories.

Surveillance for notifiable diseases. A case of a notifiable disease diagnosed at a health center is entered into a special log book. On a weekly basis, the data from this log are transferred to a form for notification of suspected transmissible diseases which is first sent to the regional health district and then to the Public Health Computer in São Paulo. The data are tabulated, and a line listing is provided to the Epidemiology Surveillance Center.

Surveillance of BPF. Because BPF is a notifiable disease in São Paulo State, criteria for diagnosis, case report forms, and instructions on how to report cases of BPF were sent to regional health districts and health centers throughout the state by means of a weekly epidemiology bulletin. In addition, several sessions on isolating *H. influenzae* biogroup aegyptius have been held to train personnel at the regional Adolfo Lutz laboratories.

During 1987 and 1988, 29 case report forms were received at the Epidemiology Surveillance Center. A definite case was defined as illness in a child that fits the case definition. A possible case was defined as fever, acute hemorrhagic skin lesions, and recent conjunctivitis in a child. In most instances, the possible cases differed from the definite cases in that tests to rule out meningococcemia had not been performed. Two cases fit the definite case definition. These involved one child from Serrana who fit the clinical criteria and another from the nearby small town of Serra Azul from whose blood *H. influenzae* biogroup aegyptius was isolated (Table 3). An additional nine children were classified as possible cases; the 11 total cases were from four towns. Six (54%) of the children died. The supporting evidence suggests that all of these children did indeed have BPF. In Votuporanga, an isolate that agglutinated with a polyclonal antiserum to a case isolate (7) was isolated from the sister of one of the children. Although this suggests that this isolate was the BPF clone, the isolate was lost before it could be further analyzed. The remaining 18 cases could not be classified as either definite or possible cases because of either incomplete data or an incompatible clinical picture.

In addition, several possible cases of BPF occurred for the first time in the city of São Paulo in April 1988. One was in a 3-year-old day care attendee who had fever, vomiting, hemorrhagic skin lesions, and a history of conjunctivitis 1 week before the onset of fever; the patient died. The BPF clone was isolated from conjunctivae of contacts of the child.

Conjunctivitis surveillance. It is important to identify BPF promptly because of the high fatality rate of BPF and the potential for epidemics. Blood cultures, however, are not routinely used for cases of suspected meningococcemia, and blood culture media are not available in all hospitals in São Paulo State. As an alternative approach, we attempted to identify outbreaks of conjunctivitis due to the BPF clone in a timely fashion to alert physicians to consider the diagnosis of BPF and to treat children with signs of systemic infection and a history of conjunctivitis promptly and aggressively. We also planned to send blood culture bottles to hospitals in areas with conjunctivitis outbreaks due to the BPF clone that normally do not have them in stock, so that an early laboratory diagnosis could be made. This would also permit personnel and resources to be mobilized to undertake important studies of BPF.

Therefore, we established a system to monitor the number of conjunctivitis cases at the health center level. Before establishing surveillance, we reviewed records in one town with an outbreak of BPF (Serrana) and two towns without known BPF (Ribeirão Preto and Cravinhos) to estimate the sensitivity and specificity of an increase in the number of conjunctivitis cases for predicting an outbreak of BPF. This review suggested that surveillance for the number of conjunctivitis cases seen per month, in conjunction with the use of the polyclonal antiserum, would be sensitive and specific for predicting BPF outbreaks.

Surveillance for conjunctivitis was established by instructing health centers to add to the weekly transmissible-disease notification form the number of cases of conjunctivitis in children <10 years old seen during that week. The Epidemiology Surveillance Center was to be notified immediately of an increase in conjunctivitis cases, arbitrarily defined as a threefold increase in the number of cases over the preceding month, to a minimum of eight cases per month. Once this threshold was reached, the conjunctivae of the next 10 to 15 children with conjunctivitis seen at the health centers were to be cultured. If the increase was due to *H. influenzae* biogroup aegyptius, the isolates were to be evaluated with the polyclonal antiserum.

We evaluated this system to determine whether it had been useful in predicting BPF outbreaks in 1987 and 1988. First, we determined whether health centers had reported the number of cases of conjunctivitis to São Paulo during at least 1 week of an arbitrarily chosen month, December 1987. In Greater São Paulo, where until recently no cases of BPF have been reported, only 6 (2%) of 373 health centers reported conjunctivitis cases. In contrast, 144 (27%) of 534 health centers in areas of the interior of the state that have not had major problems with BPF reported conjunctivitis, and 45 (36%) of 125 health centers in areas that have had BPF cases reported conjunctivitis.

To determine whether surveillance for conjunctivitis predicted BPF clusters, we reviewed the forms sent to São Paulo from the four towns reporting BPF. Of the four towns with BPF cases, only Serrana reported an increase in conjunctivitis before the first BPF case, from 4 in September to 17 each in October and November. No conjunctival cultures were taken before the first case to determine whether the increase was due to the BPF clone. It is not clear whether the failure to detect an increase in the other three towns represents a lack of reporting by the health center or a true lack of an increase in conjunctivitis. However, the sensitivity of an increase in reported conjunctivitis cases appears to be low.

To estimate the specificity of an increase in conjunctivitis cases, we reviewed forms from June through March for 17 randomly selected towns that had not reported BPF cases to determine how many of these had an increase in conjunctivitis cases. Of the 17 towns, 9 (53%) reported increases, indicating a low specificity. No conjunctival cultures were done during the times when cases increased to determine whether specificity could have been improved with the use of the agglutinating antiserum.

The sensitivity and specificity of the polyclonal agglutinating antiserum were also evaluated by using isolates that had been sent to São Paulo. The most appropriate way to determine the sensitivity of the antiserum in surveillance would be to test isolates obtained before the first case of BPF was identified in each town. Unfortunately, cultures were done only in towns with recent BPF cases after the first case, usually from case contacts. In three of the four towns, at least 50% of the isolates collected agglutinated (Table 4). Strains from two of these towns were the BPF clone; no further information is available on the isolates from the third.

TABLE 4. Evaluation of polyclonal antiserum for use in conjunctivitis surveillance

Town	No. of isolates tested	No. (%) of isolates positive[a]
With BPF		
Nova Granada	10	5 (50)[b]
Serra Azul	2	2 (100)[b]
Serrana	4	0 (0)
Votuporanga	5	3 (60)[c]
Without BPF		
Fernandópolis	6	2 (33)[d]
Guariba	13	1 (8)[d]
Promissão	17	0 (0)
Tanabí	4	0 (0)

[a] Of the isolates from all four towns with BPF and all four towns without BPF, respectively, 48 and 8% were positive.
[b] The agglutinating strains were identical to the BPF clone.
[c] The agglutinating strains were lost before further analysis.
[d] The agglutinating strains were not identical to the BPF clone.

When we evaluated the specificity by reviewing isolates collected during conjunctivitis outbreaks from towns without BPF (Table 4), two of the four towns had at least one isolate that agglutinated; none of these was the BPF clone. These limited data suggest that the currently used antiserum may not be sufficiently specific to be useful in surveillance.

Thus, several problems limit the utility of conjunctivitis surveillance. Although this system has been useful for detection of suspected BPF cases, the sensitivity of a reported increase in cases of conjunctivitis does not appear to be sufficiently high to predict most BPF outbreaks. The antiserum currently available may not improve the poor specificity of an increase in conjunctivitis cases.

Although identification of the etiology of conjunctivitis outbreaks should still be attempted, BPF surveillance must focus more heavily on the use of blood cultures for diagnosis. It is also important that a more specific rapid diagnostic test for identifying the BPF clone be developed. A population-based study of BPF in several areas of São Paulo State to define attack rates during epidemic and endemic periods would measure the morbidity and mortality due to BPF. Because it is not known where else in the world BPF may occur, clinicians and public health officials should be aware of this serious pediatric disease.

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