

# Porcine *Streptococcus suis* strains as potential sources of infections in humans: an underdiagnosed problem in North America?

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*Streptococcus suis* is a gram-positive coccus, possessing cell wall antigenic determinants related to Lancefield group D, although it is genetically unrelated to other members of this group, such as enterococci. *Streptococcus suis* is a capsulated bacterium, with the composition of the capsule defining the serotype. There are presently 35 capsular types or serotypes. The original classification of *S suis* into Lancefield groups R, S, and T is erroneous, obsolete, and should be avoided. Strains of *S suis* originally defined as Lancefield groups R, S, and T correspond to capsular types 2, 1, and 15, respectively.<sup>1</sup>

*Streptococcus suis* infection has been considered a major and worldwide problem in the swine industry, particularly during the past 15 years. The natural habitat of *S suis* is the upper respiratory tract (particularly the tonsils and nasal cavities) and the genital and alimentary tracts of pigs.<sup>2</sup> The most important clinical manifestation associated with *S suis* is meningitis. However, other pathological conditions have also been described, such as arthritis, endocarditis, pneumonia, and septicemia with sudden death.<sup>2</sup> Although *S suis* is considered primarily a swine pathogen, it has been increasingly isolated from a wide range of mammalian species, including human beings, and from birds, which suggests new concepts about some epidemiological aspects of the infection.

## Diagnosis of *S suis* infections

Presumptive diagnosis of *S suis* infections in pigs is based on clinical signs and macroscopic lesions. Confirmation of infection must be achieved by isolation of the infectious agent and recognition of microscopic

lesions in tissues.<sup>2</sup> Isolation of *S suis* from lungs must be interpreted with caution, since this organism is almost constantly present in the upper respiratory tract. Pigs may harbor a variety of *S suis* strains or serotypes in their nasal cavities and tonsils with no relationship to a specific pathological condition. It is also possible to isolate multiple *S suis* serotypes from diseased animals within the same herd.<sup>2</sup>

Veterinary diagnostic laboratories easily identify *S suis* isolates by using a minimum of biochemical tests, especially when isolates are recovered from diseased pigs. As proposed by Devriese et al,<sup>3</sup> an alpha-haemolytic *Streptococcus* recovered from diseased pigs that produces amylase, but not acetoin, may be considered *S suis*. Some laboratories proposed the use of multi-tests, such as the API Strep System test (BioMérieux, France); however, some strains of *S suis* may be misidentified using these commercial kits.<sup>4</sup> In addition, it has been proposed that, using these kits, *S suis* serotypes 1 and 2 can be differentiated on the basis of some biochemical properties, but this was shown to be untrue.<sup>4</sup> Serotyping is still an important part of the routine diagnostic procedure. Although different techniques exist, many laboratories have adopted coagglutination for serotyping.<sup>2</sup> Since the majority of typable isolates belong to capsular types 1 through 8, it is advisable for diagnostic laboratories to use only antisera corresponding to those serotypes and to send untypable isolates to a reference laboratory.<sup>2</sup>

Isolation and identification of *S suis* isolates from carrier pigs is much more complicated. In fact, most pigs harbour *S suis* in their tonsils.<sup>5</sup> Multiple serotypes, as well as untypable strains, may be present in the

same animal.<sup>5</sup> In fact, in these cases, final identification of untypable strains must be carried out by using *S suis* species-specific polymerase chain reaction (PCR) tests.<sup>6</sup> Finally, no reliable serological test has been described. Strain-specific ELISA tests may, however, be used to follow up on either maternal antibodies or active immunity (after infection or vaccination), as recently reported.<sup>7</sup>

*Streptococcus suis* has been increasingly isolated from a wide range of mammalian species, including human beings. There are some risks of misidentification of *S suis* isolates recovered from animal species other than swine. In fact, streptococci recovered from animal species other than swine may be erroneously classified as *S suis* when the identification has been carried out only on the basis of biochemical tests, since other streptococci may share similar characteristics. In addition, some of these strains may even present positive reactions when serotyped with serotype-specific anti-*S suis* sera, further complicating the diagnosis (unpublished observations). In these cases, species-specific PCR tests must be used for final identification, as for untypable strains recovered from carrier animals. Only PCR-positive strains should then be serotyped.

The opposite situation occurs when *S suis* isolates are recovered from human beings. Although the disease is sporadic, it is most probably underdiagnosed, because the causative agent may be mistaken for other organisms of similar appearance. Even though *S suis* field isolates readily grow on media employed for culturing bacteria that cause meningitis, many laboratories are not aware of *S suis*, and it is usually misidentified as enterococci, *Streptococcus pneumoniae*, *Streptococcus bovis*, viridans group streptococci, or even *Listeria monocytogenes*.<sup>8,9</sup> For example, Donsakul et al<sup>10</sup> reported that in five of eight cases, *S suis* infections had been erroneously diagnosed as *Streptococcus*

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*viridans*. In many cases, the initial gram-stain diagnosis of the cerebrospinal fluid specimen is pneumococcal meningitis. *Streptococcus suis* meningitis may have been missed in the past because of such confusion. *Streptococcus suis* infections in humans are observed more frequently in intensive pig farming areas, or where people live in close contact with pigs.<sup>11</sup> Cases have been reported in The Netherlands, Denmark, Italy, Germany, Belgium, United Kingdom, France, Spain, Sweden, Ireland, Austria, Hungary, Hong Kong, Croatia, Japan, Singapore, Taiwan, New Zealand, and Argentina.<sup>8</sup> Mysteriously, only a few cases have been reported in Canada<sup>9</sup> and none in the United States.

## ***Streptococcus suis* infection in humans**

Since the first description in Denmark in 1968,<sup>12</sup> nearly 200 human cases of *S suis* infection have been reported. Several reports indicate “Lancefield group R streptococci”; since this terminology has been abandoned, the pathogen in these cases must be regarded as *S suis*. In general, *S suis* disease is considered a rare event in man. However, it has been reported to be “one of the major causes of meningitis in adults in Hong Kong.”<sup>13</sup> Most cases are caused by serotype 2 strains, but cases due to serotype 4 (one case) and serotype 14 strains (two cases) have also been observed.<sup>14,15</sup> Two recently diagnosed *S suis* serotype 1 cases in humans remain to be confirmed, because the serotype of these strains was established only by means of biochemical criteria (API galleries) and was not confirmed with a serologic reaction using specific sera, as required for serotyping.<sup>16</sup> Unfortunately, these isolates are no longer viable to confirm the serotype (J. Kopic, personal communication, 2004).

In man, *S suis* usually produces a purulent or nonpurulent meningitis.<sup>2</sup> In addition, endocarditis, cellulitis, rhabdomyolysis, arthritis, pneumonia, and endophthalmitis have been reported. Arthritis was reported affecting various joints, including hips, elbows, wrists, sacroiliac, spine, and thumb.<sup>17</sup> In most cases, arthritis reflects generalized septicemia caused by *S suis*. Severe cases of sepsis with shock, multiple organ failure, disseminated intravascular coagulation, and associated purpura, which lead to death within hours, have also been described.<sup>18</sup> In general, activation of cytokines due to

bacteremia induces a systemic inflammatory response syndrome and arises under specific conditions, such as resistance of the host and virulence of the microbial agent. In this regard, it has been reported that *S suis* up-regulates important pro-inflammatory cytokines in human cells.<sup>14</sup> Thus, this exaggerated inflammatory mechanism may play an important role in fatal cases.

One of the most striking features of *S suis* infection in humans is the consequence of deafness following meningitis. In fact, the recorded incidence of deafness following *S suis* infection is consistently higher than that for other bacteria that cause meningitis, and may reach 50% and 65% in Europe and Asia, respectively.<sup>10</sup> The reason for this is unknown. The unilateral or bilateral, mainly high-tone deafness is frequently associated with vertigo. Early administration of antibiotics does not appear to have any influence on subsequent hearing loss. Deafness has not been reported in nonmeningitis cases of human *S suis* infection.

## **Epidemiology of *S suis* infection in humans**

The route of entry of the organism in humans may be a small cut in the skin, although in some cases, no wound was detected. Colonization of the nasopharynx, as observed in swine, or the gastrointestinal tract, suggested by observation of diarrhea as a prodromal sign, have also been suggested. The incubation period ranges from a few hours to 2 days.<sup>8</sup>

Although not all facets of the epidemiology of *S suis* infections in humans have been elucidated, it is apparent that nearly all cases may be ascribed to a high degree of exposure to unprocessed pig meat or to close contact with pigs. Since most patients acquire the disease when occupationally exposed to pigs or pork products, the preponderance of adult males is readily explained.<sup>8</sup> Manifestation of disease in pigs is not a prerequisite for infections in people in contact with pigs, since most animals are colonized by *S suis* without clinical signs.<sup>2,5</sup> In addition to domestic pigs, wild boars may also be a source of *S suis* infection for hunters and poachers.<sup>19</sup> In the United Kingdom and France, this infection has been listed as an industrial disease in 1983 and 1995, respectively.<sup>17,20</sup> Most infected people are pig farmers, abattoir workers, persons transporting pork, meat inspectors, and butchers. From studies of contamination of hands and knives, it was concluded

that eviscerators involved in removing the larynx and lungs from the carcasses have a significantly higher risk of exposure to *S suis* than other abattoir workers.<sup>21</sup> Finally, one documented case in a veterinary surgeon has been reported.<sup>17</sup> In very few cases, there was no apparent connection with exposure to pigs or pork products.<sup>11</sup>

Information about the occurrence and frequency of human colonization by *S suis* is scarce, with most data coming from abattoir workers.<sup>11,22</sup> In New Zealand, relatively high antibody titers against *S suis* serotype 2 were reported in people with occupational contact with the pig industry.<sup>23</sup> However, these data should be regarded with caution, since no standardized serological test exists to detect *S suis* antibodies. It seems evident that high exposure to *S suis* may lead to colonization of the upper respiratory tract without any health consequence. Only in some cases, clinical disease may follow. Splenectomy, and to a lesser extent, alcoholism, have been suggested as important predisposing factors for development of serious *S suis* disease.<sup>15,24</sup> The fatality rate for *S suis* infection after splenectomy seems to be approximately 80%. It has even been suggested that individuals who have had splenectomies should be excluded from the meat trade or pig farms.<sup>24</sup>

In general, *S suis* isolates from humans are phenotypically and genotypically similar to those recovered from pigs. In 2001, Tarradas et al.<sup>25</sup> reported two cases of meningitis in a butcher and an abattoir worker who handled pork meat that originated from the same three closed farms. Analysis of *S suis* serotype 2 strains recovered from tonsils of healthy pigs from those farms were genotypically similar (but not identical) to the human strains. The slight differences between isolates were probably the consequence of adaptation to the new host or simply lack of reproducibility of the detection technique. Virulence properties of strains isolated from pigs or humans seem to be similar.<sup>14</sup>

## **Therapy and prevention of *S suis* infection in humans**

*Streptococcus suis* strains recovered from human beings proved to be sensitive to penicillin in all instances except for one penicillin-tolerant strain.<sup>8</sup> Therefore, intravenous penicillin G has been a successful treatment in most cases. At least two relapses have been

reported after 2 and 4 weeks of treatment; therefore, treatment should be applied for a relatively long period of time (at least 6 weeks).<sup>26</sup> Ampicillin and chloramphenicol, sometimes combined with an aminoglycoside, may also be used. Hearing loss and vestibular disturbances are frequently observed sequelae unrelated to the antibiotic.<sup>8</sup>

*Streptococcus suis* vaccines for humans do not exist. Interestingly, recurrent septic shock due to *S suis* serotype 2, at a 15-year interval, has been reported.<sup>18</sup> The second and fatal episode was considered a re-infection rather a recurrence of the previous infection, confirming the absence of immunity after the previous infection and the utmost importance of constant prevention in exposed workers.

Despite the low incidence of *S suis* infection in humans, some preventive measures may be justified due to the high rate of contamination of pigs with this microorganism. People coming into close occupational contact with pigs or pork should pay special attention. Most infected persons are probably healthy carriers;<sup>11</sup> however, in situations of stress or immunodeficiency, *S suis* may become an opportunistic pathogen. The environment may act as source of infection, and *S suis* can survive in dust, manure, and pig carcasses for days or even weeks under optimal conditions. Moreover, *S suis* can survive in water for 10 minutes at 60°C, making the scalding process in abattoirs a possible source of contamination.<sup>11</sup> Some authors recommend prompt first-aid for injuries in meat handlers to reduce the risk of *S suis* infections,<sup>11</sup> but others consider this recommendation questionable, because skin lesions have been reported only in some cases, and the route of entry of the infection remains unclear.<sup>8</sup> Therefore, it is difficult to recommend effective prevention measures for employees of the food product industry.

## Conclusion

*Streptococcus suis* is an uncommon but serious disease in humans. Although the infection is widely distributed in the pig population, relatively few human cases are reported each year. This is probably the consequence of a low level of colonisation of human mucosae by this pathogen, a relatively low susceptibility to develop the disease of healthy persons in contact with pigs, a serious diagnostic problem in labo-

ratories working with human medicine, or all of these possibilities. In fact, most laboratories are likely to misidentify an *S suis* isolate. This is the only explanation for the lack of reports of human cases in the United States, where *S suis* is one of the most important swine pathogens. Physicians and microbiologists should be aware of this infection, especially when streptococcal meningitis is diagnosed in people working with pigs or pork products. Veterinarians should also be aware that a low but real risk may be present when manipulating *S suis*-diseased animals that are probably shedding high numbers of this zoonotic etiological agent.

## References

- Gottschalk M, Higgins R, Jacques M, Mittal KR, Henrichsen J. Description of 14 new capsular types of *Streptococcus suis*. *J Clin Microbiol*. 1989;27:2633–2636.
- Higgins R, Gottschalk M. Streptococcal diseases. In: Straw BE, D'Allaire S, Mengeling WL, Taylor DJ, eds. *Diseases of Swine*. Ames, Iowa: Iowa State University Press; 1999:563–570.
- Devriese LA, Ceysens K, Hommez J, Kilpper-Balz R, Schleifer KH. Characteristics of different *Streptococcus suis* ecovars and description of a simplified identification method. *Vet Microbiol*. 1991;26:141–150.
- Gottschalk M, Higgins R, Jacques M, Beaudoin M, Henrichsen J. Isolation and characterization of *Streptococcus suis* capsular types 9–22. *J Vet Diagn Invest*. 1991;3:60–65.
- Staats JJ, Feder I, Okwumabua O, Chengappa MM. *Streptococcus suis*: past and present. *Vet Res Commun*. 1997;21:381–407.
- Okwumabua O, O'Connor M, Shull E. A polymerase chain reaction (PCR) assay specific for *Streptococcus suis* based on the gene encoding the glutamate dehydrogenase. *FEMS Microbiol Lett*. 2003;218:79–84.
- Cloutier G, D'Allaire S, Martinez G, Surprenant C, Lacouture S, Gottschalk M. Epidemiology of *Streptococcus suis* serotype 5 infection in a pig herd with and without clinical disease. *Vet Microbiol*. 2003;97:135–151.
- Lütticken R, Temme N, Hahn E, Bartelheimer EW. Meningitis caused by *Streptococcus suis*: case report and review of the literature. *Infection*. 1986;14:181–185.
- Michaud S, Duperval R, Higgins R. *Streptococcus suis* meningitis: first case reported in Quebec. *Can J Infect Dis*. 1996;7:329–331.
- Donsakul K, Charungthai D, Witoonpanich R. *Streptococcus suis*: clinical features and diagnostic pitfalls. *Southeast Asian J Trop Med Public Health*. 2003;34:154–158.
- Strangmann E, Fröleke H, Kohse KP. Septic shock caused by *Streptococcus suis*: case report and investigation of a risk group. *Int J Hyg Environ Health*. 2002;205:385–392.
- Perch B, Kristjansen P, Skadhauge KN. Group R streptococci pathogenic for man. Two cases of meningitis and one fatal case of sepsis. *Acta Pathol Microbiol Scand B*. 1968;74:69–76.

- Chau PY, Huang CY, Kay R. *Streptococcus suis* meningitis. An important underdiagnosed disease in Hong Kong. *Med J Aust*. 1983;1:414–417.
- Gottschalk M, Segura M. The pathogenesis of the meningitis caused by *Streptococcus suis*: the unresolved questions. *Vet Microbiol*. 2000;76:259–272.
- Watkins EJ, Brooksby P, Schweiger MS, Enright SM. Septicaemia in a pig-farm worker. *Lancet*. 2001;357:38.
- Kopic J, Paradzik MT, Pandak N. *Streptococcus suis* infection as a cause of severe illness: 2 cases from Croatia. *Scand J Infect Dis*. 2003;34:683–709.
- Walsh B, Williams AE, Satsangi J. *Streptococcus suis* type 2: pathogenesis and clinical disease. *Rev Med Microbiol*. 1992;3:65–71.
- Francois B, Gissot V, Ploy MC, Vignon P. Recurrent septic shock due to *Streptococcus suis*. *J Clin Microbiol*. 1998;36:2395.
- Halaby T, Hoitsma E, Hupperts R, Spanjaard L, Lurink M, Jacobs J. *Streptococcus suis* meningitis, a poacher's risk. *Eur J Clin Microbiol Infect Dis*. 2000;19:943–945.
- Pedroli S, Kobisch M, Beauchet O, Chaussinand JP, Lucht F. Bactériémie à *Streptococcus suis* [Streptococcus suis bacteremia]. *La Presse medical*. 2003;32:599–601.
- Breton J, Mitchell WR, Rosendal S. *Streptococcus suis* in slaughter pigs and abattoir workers. *Can J Vet Res*. 1986;50:338–341.
- Sala V, Colombo A. Infection risks of *Streptococcus suis* type 2 localizations in slaughtered swine. *Arch Vet It*. 1989;40:180–184.
- Robertson ID, Blackmore DK. Occupational exposure to *Streptococcus suis* type 2. *Epidemiol Infect*. 1989;103:157–164.
- Gallagher F. *Streptococcus suis* infection and splenectomy. *Lancet*. 2001;357:1131–1132.
- Tarradas C, Luque I, de Andres D, Abdel-Aziz Shahein YE, Pons P, Gonzalez F, Borge C, Perea A. Epidemiological relationship of human and swine *Streptococcus suis* isolates. *J Vet Med B*. 2001;48:347–355.
- Woo J, Li EK. *Streptococcus suis* meningitis requires prolonged treatment with penicillin. *Infection*. 1987;15:129.

