Human *Streptococcus suis* Infections in Thailand: Epidemiology, Clinical Features, Genotypes, and Susceptibility

Anusak Kerdsin

Faculty of Public Health, Kasetsart University, Chalermprakiat Sakon Nakhon Province Campus, Sakon Nakhon 47000, Thailand; anusak.ke@ku.th

Abstract: *Streptococcus suis* is a zoonotic pathogen causing substantial economic losses to the pig industry, as well as being a human health burden due to infections worldwide, especially in Southeast Asia. In Thailand, there was high cumulative incidence in humans during 1987–2021, mostly in males. At least five large outbreaks have been documented after the largest outbreak in China in 2005, which was related to the consumption of raw pork or dishes containing pig’s blood. The major clinical features are sepsis or meningitis, with hearing loss a major complication of *S. suis* disease. Thai human *S. suis* isolates have shown diversity in serotypes and sequence types (STs), with serotype 2 and STs 1 and 104 being major genotypes. β-Lactam antibiotics can be used in empirical treatment for human *S. suis* infections; however, intermediate resistance to penicillin has been reported. Reducing *S. suis* incidence in Thailand requires a multidimensional approach, with combined efforts from the government and public health sectors through policy, regulations, education, and active surveillance.

Keywords: *Streptococcus suis*; serotype; sequence type; susceptibility; outbreak; Thailand

1. Introduction

*Streptococcus suis* is a Gram-positive coccus bacterium responsible for major infections in pigs and significant economic losses in the pig industry worldwide. The most important clinical manifestations associated with *S. suis* infection in pigs are meningitis, arthritis, endocarditis, pneumonia, rhinitis, abortion, and vaginitis [1]. It is also an emerging zoonotic pathogen causing serious diseases in humans, including meningitis, sepsis, septic shock, infective endocarditis, and septic arthritis [1,2]. The number of reported human *S. suis* cases has substantially increased, with Southeast Asian countries leading the counts, especially Thailand and Vietnam [1–3]. Occupations related to pigs or pork, exposure to pig or pork products, or the consumption of raw pork products are the main risk factors of human infection [1,3].

*S. suis* is an encapsulated pathogen, with the capsular polysaccharide antigens being the basis for classification into serotypes [1]. Among 29 serotypes, serotype 2 is considered the most pathogenic and a frequent cause of human disease worldwide [1]. In Western countries, such as the United Kingdom, Spain, Germany, the Netherlands, Canada, and the United States, as well as in Japan, China, and Hong Kong, most human *S. suis* cases have occurred after occupational exposure involving pig handling among pig farmers, bleeders, abattoir workers, carcass cutting and processing workers, butchers, and cooks [3]. However, in Southeast Asian countries, such as Thailand, Vietnam, and Indonesia, a nontrivial number of human cases has occurred in individuals consuming meals containing raw pork meat, blood, and other related products [3]. Two studies in Thailand showed that *S. suis* human infections were responsible for an estimated loss in productivity-adjusted life years to the gross domestic product of USD11.3 million, which equates to USD36,033 lost per person and out-of-pocket expenses for individuals and their families that averaged USD140 (GBP104 or THB5198) per patient [4,5].

In this review, we focus on *S. suis* infections in Thai humans based on epidemiology, clinical manifestations, genotypes, and susceptibility to antimicrobials. Thailand’s high
incidence of human *S. suis* cases can provide information for policy implementation, active surveillance, and prevention of this disease.

2. Epidemiology of Human *S. suis* Infections in Thailand

In Thailand, *S. suis* infection was first described in 1987 in Bangkok, with two cases of meningitis [6]. Before the largest outbreak of human *S. suis* infection occurred in Sichuan province, China in 2005 [7], sporadic human cases had been reported in several provinces in Thailand, especially in the north [8–14]. One outbreak with 10 fatal cases due to septic shock was documented in 2000 in Lamphun province, northern Thailand, well before the largest outbreak occurred in China [14]. That study demonstrated that all cases were healthy men aged 40–49 years who were clustered during the same period and geographic area [14]. All cases had a history of chronic alcohol use and the consumption of raw pork or pig’s blood dishes prior to their illness [14]. Notably, all cases in that study had clinical symptoms similar to the cases in the Sichuan outbreak in China in 2005 [7,14].

After the Sichuan outbreak in China, the importance of this disease has been increasingly recognized in Thailand, as well as in many countries worldwide. Up to the present, five large outbreaks of *S. suis* infections in humans have been documented in Thailand: four of these outbreaks were in the north, whereas a fifth outbreak occurred in the northeast. The first outbreak, comprising 29 laboratory-confirmed cases and 3 deaths, occurred in Phayao province during May 2007 [15]. A second outbreak was recognized in Chiang Mai and Lamphun provinces during June–July 2008, with 44 confirmed cases, 26 suspected cases, and 3 fatal cases with septic shock [16]. The third outbreak was reported in Phetchabun province in April 2010, with 14 confirmed cases, of which 5 were fatal [2]. The fourth outbreak was reported in Uttaradit province in May 2019, with 5 confirmed cases and 18 suspected cases [17]. A fifth outbreak occurred for the first time in northeastern Thailand (Nakhon Ratchasima) in 2021, with 21 confirmed cases, including 2 fatal cases [18]. Microbiological analysis of the outbreak *S. suis* strains showed that the first and second outbreaks were due to serotype 2 with sequence type (ST) 1, while the third outbreak was caused by serotype 2-ST104 and serotype 14-ST105. There was no available information about the serotype and STs in the fourth outbreak. The fifth outbreak was caused by serotype 2 with a new ST (ST1656) belonging to the clonal complex (CC) 233/379 [18].

National guidelines for human *S. suis* infections are not yet available in Thailand. However, the practice of *S. suis* recruitment in the public health system is conducted using the R506 system (a daily case report of communicable diseases) of the Ministry of Public Health that was initiated after the first large outbreak in 2007. As shown in Figure 1, human cases reported in the system showed an increasing trend during 2011–2021. Although the number of cases dropped in 2022, annual data were only up until September. Notably, these reported cases were submitted by the hospital network where they could identify this bacterium. Thus, misidentification of *S. suis* as other bacteria might have occurred, and this would not have been reported in that system [19–22]. Therefore, the reported human *S. suis* cases registered in the R506 system may be lower than the real situation.

The national annual crude incidence is 0–0.381 per 100,000 persons [22]. A study in Nakhon Phanom province (northeastern Thailand) documented an annual incidence of 0.1–2.2 cases per 100,000 population for 2006–2012 [22]. This differed from a study in 2010 that estimated human cases to be 730 per year in northern Thailand, with an incidence of 6.2 per 100,000 of the general population [23]. The reasons for these different rates are still unknown, but ethnicity, tribe, cultural behavior, and lifestyle might all influence the *S. suis* infection rate [3].

Three retrospective studies reported that the incidence of *S. suis* disease was high during the rainy season (June–September) [24–26]. In contrast, a prospective study in Phayao province, Thailand showed peak incidence in summer (April and May) [23]. In addition, all five outbreaks discussed above occurred in summer. Almost all cases were related to the Songkran Festival (a traditional Thai New Year festival in Thailand) and other harvesting festivals during summer [3].
Several studies revealed that adult age, male sex, alcohol drinking, pig-related occupation or exposure, and raw pork consumption were common risk factors of \textit{S. suis} infections in Thailand \cite{15,27,28}. However, two meningitis cases in children caused by \textit{S. suis} have also been reported in this country \cite{9,29}. The first case was infected with an unknown serotype and ST and the second case was caused by serotype 24 with ST221 \cite{9,29}. Overall, mortality of \textit{S. suis} infections in Thailand is in the range 9.5–19.5\% \cite{4,13,24–26,30}. Several studies in Thailand have shown that fatal risk factors include septic shock, rapid onset of illness, prolonged bacteremia $\geq$ 6 days, low serum albumin, high serum total bilirubin, low platelet count, and elevated alanine transaminase \cite{13,26,30}. In particular, septic shock is a strong risk factor, being 22-folds greater than in non-septic shock patients \cite{30}.

3. Clinical Features of Thai Human \textit{S. suis} Infections

This review collected all reported papers written in either Thai or English that documented \textit{S. suis} infections in Thailand from the available online databases (PubMed, ScienceDirect, Scopus, Google, Thai Index Medicus of Chulalongkorn University, and Siriraj Hospital, Bureau of Epidemiology). Search terms were \textit{S. suis}, human, clinical, Thai, Thailand, outbreak, all years.

In total, 1798 cases from 59 reports were identified \cite{6,8–18,21–26,28–68}. Most cases were male ($n = 1287$). Among the 1798 cases, 1052 involved consumption and/or exposure to pig or raw pork products. Septicemia and meningitis were predominant clinical manifestations and hearing loss was a major complication. All this information is summarized in Table 1. According to the retrospective and prospective studies, septicemia/sepsis and meningitis were the most common clinical features found in Thai patients \cite{23–26}.

\begin{table}[h]
\centering
\caption{Characteristics of human \textit{Streptococcus suis} cases in Thailand 1987–2021.}
\begin{tabular}{|c|c|}
\hline
\textbf{Characteristic} & \textbf{Number of Cases} \\
\hline
Total cases & 1798 \\
\hline
\end{tabular}
\end{table}
| Characteristic                                      | Number of Cases |
|----------------------------------------------------|-----------------|
| **Sex (n = 1679)**                                 |                 |
| Male                                               | 1287 (76.6%)    |
| Female                                             | 392 (23.4%)     |
| **Ratio of male-to-female**                        | 3.3:1           |
| **Age range (years)**                              | 0.15–92         |
| **Occupation (n = 288)**                           |                 |
| Farmer/gardener                                    | 153 (53.1%)     |
| Worker/laborer                                     | 71 (24.6%)      |
| Employee/officer (government or private)           | 45 (15.6%)      |
| Butcher                                            | 12 (4.2%)       |
| Cook                                               | 4 (1.4%)        |
| Housewife                                          | 3 (1.1%)        |
| **Risk behavior (n = 1430)**                       |                 |
| Consumption of raw pork/pig’s blood dishes         | 878 (61.4%)     |
| Exposure to pig/raw pork products                  | 139 (9.7%)      |
| Raw pork product consumption and pig/raw pork exposure | 35 (2.5%)   |
| Alcohol drinking/alcoholism                        | 362 (25.3%)     |
| No history of pig/raw pork contact or consumption  | 16 (1.1%)       |
| **Outcome (n = 1798)**                             |                 |
| Alive                                              | 1438 (80%)      |
| Dead                                               | 218 (12.1%)     |
| No information                                     | 142 (7.9%)      |
| Fatality rate                                      | 12.1%           |
| **Clinical presentation/type of infection (n = 1736)** |             |
| Meningitis                                         | 709 (40.8%)     |
| Meningitis and septic arthritis                    | 12 (0.7%)       |
| Meningitis and spondylodiscitis                    | 1 (0.06%)       |
| Spondylodiscitis                                   | 19 (1.1%)       |
| Septicemia/sepsis                                  | 748 (43.1%)     |
| Septic shock                                       | 67 (3.8%)       |
| Infective endocarditis                             | 111 (6.4%)      |
| Septic arthritis                                   | 51 (2.9%)       |
| Peritonitis                                        | 6 (0.4%)        |
| Pneumonia/pulmonary edema                          | 5 (0.3%)        |
| Endophthalmitis                                    | 4 (0.2%)        |
| Cellulitis                                         | 1 (0.06%)       |
| Acute suppurative thyroiditis                      | 1 (0.06%)       |
Table 1. Cont.

| Characteristic                                    | Number of Cases |
|--------------------------------------------------|-----------------|
| Cholecystitis                                    | 1 (0.06%)       |
| Complication (n = 432)                           |                 |
| Hearing loss or deafness                         | 324 (75%)       |
| Acute respiratory distress syndrome (ARDS)      | 23 (5.3%)       |
| Acute renal failure                              | 23 (5.3%)       |
| Disseminated intravascular coagulation (DIC)    | 19 (4.4%)       |
| Ataxia                                           | 12 (2.7%)       |
| Shock                                            | 11 (2.5%)       |
| Cranial nerve palsy                              | 5 (1.2%)        |
| Hemiparesis/paralysis                            | 4 (0.9%)        |
| Congestive heart failure                         | 3 (0.7%)        |
| Papilledema                                      | 3 (0.7%)        |
| Intracerebral hemorrhage                         | 2 (0.5%)        |
| Subdural empyema                                 | 1 (0.2%)        |
| Intervertebral discitis                          | 1 (0.2%)        |
| Stroke                                           | 1 (0.2%)        |
| Predisposition (n = 455)                         |                 |
| Diabetes mellitus                                | 53 (11.6%)      |
| Hypertension                                     | 53 (11.6%)      |
| Heart disease                                    | 46 (10.1%)      |
| Spondylitis                                      | 27 (5.9%)       |
| Systemic lupus erythematosus (SLE)               | 21 (4.6%)       |
| Dyslipidemia                                     | 16 (3.5%)       |
| Adrenoleukodystrophy (ALD)                       | 16 (3.5%)       |
| Liver cirrhosis                                  | 13 (2.9%)       |
| Gout/rheumatoid                                  | 4 (0.9%)        |
| Splenectomy                                      | 2 (0.4%)        |
| Cancer                                           | 2 (0.4%)        |
| HIV/AIDS                                         | 2 (0.4%)        |
| Down syndrome                                    | 1 (0.2%)        |
| Thyroid                                          | 1 (0.2%)        |
| Anemia                                           | 1 (0.2%)        |
| Spinal canal stenosis                            | 1 (0.2%)        |
| Unspecified or other underlying diseases         | 16 (3.5%)       |
| No predisposing factors/healthy                  | 180 (39.6%)     |

4. Genotypes of Thai Human S. suis Strains

As shown in Table 2, for S. suis isolated from patients in Thailand, serotype 2 (93.4%) was dominant, followed by serotypes 14 (5.2%), 24 (0.6%), 5 (0.4%), 4 (0.1%), 9 (0.1%), 31 (0.1%), and unencapsulated (0.1%), respectively [21,24,25,32,69]. MLST classified serotype 2 into five CCs: CC1, CC25, CC28, CC104, and CC233/379. Of these, CC1 is a major CC of human S. suis infection in this country and ST1 is the main ST in CC1 [25], while serotype
14 was classified to only CC1, with ST105 predominant [25,69]. For serotype 2, ST104, ST25, ST28, and ST233 were the main STs in CC104, CC25, CC28, and CC233/379, respectively. Notably, STs 1 and 104 for serotype 2 are the predominant STs in Thai human infections, and CC104, CC233/379, and CC221/234 are found exclusively in Thailand [24,25,70].

| Serotype | Clonal Complex | Sequence Type | Reference |
|----------|----------------|---------------|-----------|
| 2        | 1              | 1, 11, 105, 126, 144, 298, 337 |
|          | 25             | 25, 102, 103, 380, 381, 395, 515, 516 |
|          | 28             | 28, 382 |
|          | 104            | 101, 104, 391, 392, 393, 512, 513, 514 |
|          | 233/379        | 233, 379, 1656, 1713 |
|          | 1687/1688      | 1687, 1688 |
|          | Singleton      | 232, 236 |
| 4        | 94             | 94 |
| 5        | 221/234        | 221 |
|          | Singleton      | 181, 235 |
| 9        | 16             | 16 |
| 14       | 1              | 11, 105, 127 |
| 24       | 221/234        | 221, 234 |
| 31       | 221/234        | 221 |
| Unencapsulated serotype 2 or 1/2 | 28 | 28 |

Table 2. Distribution of genotypes of \textit{S. suis} isolates from humans.

Two retrospective studies revealed that the ST1 strains were more associated with meningitis than the other STs [24,25]. However, the ST104 strains were more associated with non-meningitis, especially sepsis [24]. Differences in clinical manifestations caused by either ST1 or ST104 may have been influenced by genetic backgrounds. Genomic comparison between ST1 and ST104 strains identified that \textit{salK/salR}, the \textit{srtBCD} gene cluster, \textit{revS}, \textit{rgg}, \textit{epf}, and a putative virulence factor SSU0835 (an ABC-type multidrug transport system), with the latter described as being involved in the invasion of porcine brain microvascular endothelial cells, were absent in ST104 [71]. Another study showed ST104 strains failed to develop high levels of meningitis in a mouse model due to low or no production of sulyisin by a negligible level of transcription of the \textit{sly} gene and undetectable \textit{sly} promoter activities [72]. That study also illustrated the contribution of sulyisin to the development of meningitis by ST1 [72]. These results may explain why ST104 caused less meningitis than sepsis.

Although most cases of Thai human \textit{S. suis} infections had a history of consumption of raw pork dishes, there was no direct evidence or laboratory investigation to confirm or prove the \textit{S. suis} strains in the raw pork dishes that were eaten because none of the raw pork dishes remained after consumption. Indirect investigation was conducted with \textit{S. suis} isolated from slaughterhouse pigs. Three studies showed \textit{S. suis} strains isolated from pigs in Thailand had genotypic profiles of PFGE, RAPD, MLST or combined techniques identical to the \textit{S. suis} strains from humans [73–75]. For example, Kerdsin and colleagues (2020) demonstrated that 70.4% of isolates of \textit{S. suis} serotypes 2 and 14 from slaughterhouse pigs revealed STs and PFGE patterns identical to the human isolates [73]. For example, Kerdsin and colleagues (2020) demonstrated that 70.4% of isolates of \textit{S. suis} serotypes 2 and 14 from slaughterhouse pigs revealed STs and PFGE patterns identical to the human isolates [73]. Similarly to Maneerat et al. (2013), the finding showed most of \textit{S. suis} serotype 2 isolates collected from human patients and pigs (diseased and asymptomatic) in different regions of Thailand had the same of ST, RAPD, and virulence-associated gene profile [74]. Such indirect evidence
suggests the genetic relationships and confirms the possibility of zoonotic transmission of S. suis isolates from pigs to humans for certain STs, especially ST1 and ST104, as well as proving that slaughterhouse pigs are a reservoir of pathogenic human S. suis strains.

5. Antimicrobial Susceptibility

Other studies have revealed that Thai S. suis isolates were susceptible to penicillin [13]. This contrasted with Nakaranurack et al. (2017), who reported that 6 out of 11 Thai S. suis isolates were immediately resistance to penicillin, whereas cefotaxime and vancomycin were completely susceptible [35]. However, a study in 2021 demonstrated that 448 S. suis isolates recovered from human infections in Thailand had 8.2% intermediate resistance to penicillin, while they were all susceptible to cefepime and ceftriaxone [76]. One study revealed penicillin-resistant S. suis with a high minimal inhibitory concentration (MIC) value of >32 μg/mL [77]. Most of the intermediate penicillin-resistant isolates belonged to serotype 2-ST233 [76]. This contrasted with worldwide human S. suis isolates showing susceptibility to β-lactam antibiotics, including penicillin, ampicillin, amoxicillin, cefotaxime, ceftriaxone, cefepime, meropenem, and imipenem [78–82]. Although there is worldwide usage of β-lactams in pigs and humans, almost all human S. suis isolates remain susceptible to this antimicrobial class.

Resistance to tetracycline (98.2%), clindamycin (94%), erythromycin (92.4%), and azithromycin (82.6%) with the resistance genes tet(O) and ermB were the predominant determinants of tetracycline and erythromycin (also macrolide-lincosamide–streptogramin B (MLSb)) resistance detected in 448 S. suis isolates [76]. Resistance to tetracycline appeared common in S. suis from human infections worldwide [78–82], whereas the resistance rates to erythromycin were low in Poland, Hong Kong, and Vietnam [78,79,83]. Although tet(O) is prevalent in human S. suis in Thailand, the tet(M) gene is the most widespread in human S. suis in China and Vietnam [79,81]. The ermB gene was predominant in human isolates in Vietnam and Thailand, while mefA was present in Hong Kong [76,79]. This may indicate differences in the local spread of tetracycline and erythromycin-resistance genes among human S. suis isolates in different countries or geographical regions.

A recent study investigated an emerging S. suis ST1656 belonging to CC233/379 that caused the fifth outbreak in Thailand carried the MLSb resistance gene ermA and the oxazolidinone and phenicol resistance gene optrA that were found exclusively in the outbreak isolates other than tet(O) and ermB [18].

6. Public Health Control

Kerdsin et al. (2022) mentioned that sociocultural factors, including cultural, religious, and societal behaviors and attitudes associated with the consumption of raw pork or pig’s blood play an important role in human infections [3]. Therefore, effecting a reduction in the human S. suis cases in Thailand requires a multidimensional approach involving the government and community sectors. Enforcement is required of meat inspection regulations and hygiene practices at pork processing facilities, as well as conducting food safety campaigns, establishing an educational program on preventing this infection, and reducing behavior regarding the consumption of raw pork or pig’s blood dishes.

Another study in Thailand showed the effectiveness of a food safety campaign [42]. Overall, this campaign led to a marked decrease in the annualized incidence of human S. suis disease, from 6.4/100,000 persons in 2010 (before the campaign implementation) to 2.7/100,000 persons in 2011, then to 2.0/100,000 persons in 2012, and finally to 3.5/100,000 persons in 2013 [42]. Finally, early diagnostics in S. suis suspected patients using rapid alternative methods rather than traditional culture (a gold standard but slower) could facilitate prompt treatment and reduce the mortality rate, as well as prompt epidemiological investigation [84–87].
7. Conclusions and Perspectives

Thailand has the second-highest number of reported human \textit{S. suis} cases, accounting for 11% of all reported cases worldwide [88]. \textit{S. suis} infections in Thailand had a very high cumulative incidence during 1987–2021, with males being represented in most cases due to them more commonly consuming raw pork or pig’s blood dishes than females. The consumption of raw pork/pig’s blood dishes is common in Thailand, especially in the north. At least five large outbreaks have been documented in Thailand along with the largest reported outbreak in Sichuan, China in 2005, and have been related to the consumption of raw pork/pig’s blood dishes. However, the first large outbreak in Thailand was apparently in 2000. The most common clinical features are sepsis or meningitis, while hearing loss is a major complication of \textit{S. suis} disease.

Thai human \textit{S. suis} isolates have diversified in serotypes and STs, with serotype 2 and STs 1 and 104 being the majority in Thailand. In addition, serotype 14 with ST105 is also prevalent in the country. \(\beta\)-Lactam antibiotics can be used in empirical treatment for human \textit{S. suis} infections; however, intermediate resistance to penicillin has been reported. This should be of concern and should be carefully monitored. Thai \textit{S. suis} strains have been reported to be highly resistant to macrolide and tetracycline.

Reducing human \textit{S. suis} disease in Thailand requires a multidimensional approach combining government and public health efforts through policy, regulations, and education, and active community involvement to effect behavioral changes that are evidence-based but culturally sensible and acceptable, along with the implementation in health-care systems of more rapid diagnostics and more relevant screening tools. Most hospital laboratories in Thailand are not able to confirm \textit{S. suis}, and consequently the infection might be misdiagnosed. Improving the capacity of hospital laboratories to identify \textit{S. suis} will aid clinical management, facilitate outbreak detection and response, and facilitate the swift initiation of control measures.

\textbf{Funding:} This research received no external funding.

\textbf{Institutional Review Board Statement:} Not applicable.

\textbf{Informed Consent Statement:} Not applicable.

\textbf{Data Availability Statement:} Not applicable.

\textbf{Acknowledgments:} The Kasetsart University Research and Development Institute (KURDI), Bangkok, Thailand provided English-editing assistance.

\textbf{Conflicts of Interest:} The authors declare no conflict of interest.

\textbf{References}

1. Goyette-Desjardins, G.; Auger, J.P.; Xu, J.; Segura, M.; Gottschalk, M. \textit{Streptococcus suis}, an important pig pathogen and emerging zoonotic agent—a update on the worldwide distribution based on serotyping and sequence typing. \textit{Emerg. Microbes. Infect.} 2014, 3, e45. [CrossRef] [PubMed]

2. Segura, M.; Aragon, V.; Brockmeier, S.L.; Gebhart, C.; De Greeff, A.; Kerdsin, A.; O’Dea, M.A.; Okura, M.; Saléry, M.; Schultsz, C.; et al. Update on \textit{Streptococcus suis} Research and Prevention in the Era of Antimicrobial Restriction: 4th International Workshop on \textit{S. suis}. \textit{Pathogens} 2020, 9, 374. [CrossRef] [PubMed]

3. Kerdsin, A.; Segura, M.; Fittipaldi, N.; Gottschalk, M. Sociocultural Factors Influencing Human \textit{Streptococcus suis} Disease in Southeast Asia. \textit{Foods} 2022, 11, 1190. [CrossRef]

4. Thongsawad, S. Burden and Epidemiological Characterisations of \textit{Streptococcus suis} in Chiang Mai, Thailand. Ph.D. Thesis, The University of Edinburgh, Edinburgh, UK, 2016.

5. Rayanakorn, A.; Ademi, Z.; Liew, D.; Lee, L.-H. Burden of disease and productivity impact of \textit{Streptococcus suis} infection in Thailand. \textit{PLoS Negl. Trop. Dis.} 2021, 15, e0008985. [CrossRef] [PubMed]

6. Phuapradit, P.; Boongird, P.; Boonyakarmkul, S.; Niramarnsakul, S.; Ponglikitmongkol, S.; Vorachit, M. Meningitis caused by \textit{Streptococcus suis} in humans. \textit{Intern. Med.} 1987, 3, 120–122.

7. Yu, H.; Jing, H.; Chen, Z.; Zheng, H.; Zhu, X.; Wang, H.; Wang, S.; Liu, L.; Zu, R.; Luo, L.; et al. \textit{Streptococcus suis} study groups. Human \textit{Streptococcus suis} outbreak, Sichuan, China. \textit{Emerg. Infect. Dis.} 2006, 12, 914–920. [CrossRef]

8. Teekakirikul, P.; Wiwanitkit, V. \textit{Streptococcus suis} infection: Overview of case reports in Thailand. \textit{S. Asian J. Trop. Med. Public Health} 2003, 34 (Suppl. 2), 178–183.
36. Kerdsin, A.; Dejriulert, S.; Sawpananyalert, P.; Boonmark, A.; Noithachang, W.; Sryakum, D.; Simkum, S.; Chokngam, S.; Gottschalk, M.; Akeda, Y.; et al. Sepsis and spontaneous bacterial peritonitis in Thailand. *Lancet* 2011, 378, 960. [CrossRef]

37. Kerdsin, A.; Takeuchi, D.; Gottschalk, M.; Hamada, S.; Akeda, Y.; Oishi, K. A human case of *Streptococcus suis* infection caused by an unencapsulated strain. *JMM Case Rep.* 2014, 1, e002329. [CrossRef]

38. Kerdsin, A.; Hatrongjit, R.; Gottschalk, M.; Takeuchi, D.; Hamada, S.; Akeda, Y.; Oishi, K. Emergence of *Streptococcus suis* serotype 9 infection in humans. *J. Microbiol. Immunol. Infect.* 2017, 50, 545–546. [CrossRef] [PubMed]

39. Pachirat, O.; Taksinachanekit, S.; Moobtsikapun, P.; Kerdsin, A. Human *Streptococcus suis* Endocarditis: Echocardiographic Features and Clinical Outcome. *Clin. Med. Insights Cardiol.* 2012, 6, 119–123. [CrossRef] [PubMed]

40. Thayawiwat, C.; Witchaiham, O.; Painpringam, A. Epidemiology of *Streptococcus suis* infections: Patients of Chiang Kham hospital, 2009-2011. *J. Health Sci.* 2012, 58, 575–588.

41. Rusmeechan, S.; Sribusara, P. *Streptococcus suis* meningitis: An emerging infectious disease of this decade. *Buddhachinaraj Med. J.* 2017, 34, 211–218.

42. Takeuchi, D.; Kerdsin, A.; Akeda, Y.; Chiranairadul, P.; Loetthong, P.; Tanburawong, N.; Areeratana, P.; Puangmali, P.; Nakayama, T.; Yamamoto, K.; et al. Impact of a Food Safety Campaign on *Streptococcus suis* Infection in Humans in Thailand. *Am. J. Trop. Med. Hyg.* 2017, 96, 1370–1377. [CrossRef]

43. Tonesanot, P. A study of *Streptococcus suis* infections in hospitalized patients in Sa Kaeo. *Chula J. Intern. Med.* 2018, 31, 50–65.

44. Rayanakorn, A.; Katip, W.; Lee, L.H.; Oberdorfer, P. Endophthalmitis with bilateral deafness from disseminated *Streptococcus suis* infection. *BMJ Case Rep.* 2019, 12, e228501. [CrossRef]

45. Jariyawattanarat, V.; Chantharit, P.; Sritara, C.; Chansoon, T.; Sriraphradang, C. A case of acute suppurative thyroiditis caused by *Streptococcus suis* infection. *Germs* 2021, 11, 592–596. [CrossRef] [PubMed]

46. Mankong, C. Permanent Deafness Due to *Streptococcus suis* Infection in Kamphaengphet Hospital. Kamphaengphet Hosp. J. n.d.

47. Pawan, V.; Areechokchai, D.; Tonghong, A.; Lortheeranuwat, A.; Yapa, R. Outbreak verification summary, 15th Week, 6–12 April 2008. *Wkly. Epidemiol. Surveill. Rep.* 2008, 39, 263. (In Thailand)

48. Rungphueng, A.; Harnchaoworakul, W.; Vagus, A.; Sakulngam, J.; Phurahong, S. Outbreak verification summary, 16th Week, 13–19 April 2008. *Wkly. Epidemiol. Surveill. Rep.* 2008, 39, 279. (In Thailand)

49. Prasarnthong, R.; Tonghong, A.; Leela, T. Outbreak verification summary, 29th Week, 13–19 July 2008. *Wkly. Epidemiol. Surveill. Rep.* 2008, 39, 514–516. (In Thailand)

50. Diregpoke, B. Outbreak verification summary, 33rd Week, 10–16 August 2008. *Wkly. Epidemiol. Surveill. Rep.* 2008, 39, 588. (In Thailand)

51. Jirapongs, C.; Kabphirom, T.; Thepsitth, K.; Phanwadee, M.; Henprasertthae, N.; Tonghong, A. Outbreak verification summary, 32nd Week, 8–14 August 2010. *Wkly. Epidemiol. Surveill. Rep.* 2010, 41, 513–514. (In Thailand)

52. Vorapani, P.; Sungkot, A.; Kungvan, C.; Nongphan, A.; Phopiam, M. Cluster of *Streptococcus suis* death, Kongkrailas district, Sukhothai province, December 2009. *Wkly. Epidemiol. Surveill. Rep.* 2010, 41, 653–656. (In Thailand)

53. Kabphirom, T.; Naruephonjirakul, U.; Yodkhao, A.; Chanthasiriyakorn, S. Outbreak verification summary, 1st Week, 2–8 January 2011. *Wkly. Epidemiol. Surveill. Rep.* 2011, 42, 6. (In Thailand)

54. Lorpiyanond, T.; Duangnern, P.; Siriarayaporn, P.; Chanthasiriyakorn, S.; Diregpoke, B.; Suwannachairop, O. Outbreak verification summary, 17th Week, 24–30 April 2011. *Wkly. Epidemiol. Surveill. Rep.* 2011, 42, 265–266. (In Thailand)

55. Thanond, J.; Suwannachairop, O.; Diregpoke, B.; Siriarayaporn, P. Outbreak verification summary, 20th Week, 15–21 May 2011. *Wkly. Epidemiol. Surveill. Rep.* 2011, 42, 313–314. (In Thailand)

56. Chanthasiriyakorn, S.; Wangtheeraprasert, T.; Yingyong, T. Outbreak verification summary, 25th Week, 19–25 June 2011. *Wkly. Epidemiol. Surveill. Rep.* 2011, 42, 392–393. (In Thailand)

57. Chaiuwatwong, S.; Monphangtheam, K.; Rattanarith, P.; Thammawichaya, P. Outbreak verification summary, 5th Week, 29 January–4 February 2012. *Wkly. Epidemiol. Surveill. Rep.* 2012, 43, 70–71. (In Thailand)

58. Prangkratoak, S.; Srisomboon, N.; Tamard, A.; Insean, W.; Siriarayaporn, P. Outbreak verification summary, 10th Week, 3–9 March 2013. *Wkly. Epidemiol. Surveill. Rep.* 2013, 44, 153–155. (In Thailand)

59. Rungseewong, S.; Worasalisri, P.; Onsongchan, S.; Kananchaphibunwong, A. Outbreak verification summary, 39th Week, 22–28 September 2013. *Wkly. Epidemiol. Surveill. Rep.* 2013, 44, 618–618. (In Thailand)

60. Kanchanasonbut, H.; Yimjohoa, N.; Thanond, J.; Sirirunggueng, A.; Siriarayaporn, P. Outbreak verification summary, 17th Week, 27 April–3 May 2014. *Wkly. Epidemiol. Surveill. Rep.* 2014, 45, 260–263. (In Thailand)

61. Kulawong, S.; Sathawornwiwat, A.; Toan, W.; Buathlon, R. Outbreak verification summary, 34th Week, 24–30 August 2014. *Wkly. Epidemiol. Surveill. Rep.* 2014, 45, 534–535. (In Thailand)

62. Sutthachana, S.; Sangchanthip, A.; Samitsuwan, P.; Chanthasiriyakorn, S.; Sukkasame, K.; Phetsindechakul, N.; Siriwatthanasopha, N.; Khampa, V.; Pramanucharuenkit, J.; Panchangamphathana, A.; et al. Outbreak verification summary, 18th Week, 1–7 May 2016. *Wkly. Epidemiol. Surveill. Rep.* 2016, 47, 277–279. (In Thailand)

63. Krobrakulchai, S.; Tunchiangsai, K.; Suthachana, S.; Thepsittha, K.; Kumphol, P.; Sukham, S.; Sukkhavej, S.; Lengie, W.; Phunkul, S.; Nakaraj, B.; et al. Outbreak verification summary, 34th Week, 21–27 August 2016. *Wkly. Epidemiol. Surveill. Rep.* 2016, 47, 536–538. (In Thailand)
64. Chanpen, O.; Surinsak, W.; Sittiprapa, W.; Jullanan, W. Investigation of Streptococcus suis death, Salalumduan subdistrict, Mueang district, Sakaeo province, Thailand, May 2016. *Wkly. Epidemiol. Surveill. Rep.* 2017, 48, 401–406. (In Thailand)

65. Wijitrphan, T.; Immoont, A. An outbreak investigation of Streptococcus suis infection, Maewang District, Chiang Mai Province, Thailand, June 2017. *Wkly. Epidemiol. Surveill. Rep.* 2017, 48, 529–536. (In Thailand)

66. Srisupap, W.; Narueponjurakul, U.; Suttawong, T.; Swaddiwudhipong, W. A case investigation of Streptococcus suis infection in a patient with total knee arthroplasty, Thephahar District, Nakhon Ratchasima Province, Thailand, August 2018. *Wkly. Epidemiol. Surveill. Rep.* 2019, 50, 17–23. (In Thailand)

67. Somboon, T.; Promduangsi, P.; Arpakhapakul, J.; Kekarakrungrungreung, N.; Sukpan, S.; Khamjai, N. An outbreak investigation of Streptococcus suis infection, Lamphun province, Thailand, August 2020. *Wkly. Epidemiol. Surveill. Rep.* 2021, 52, 389–398. (In Thailand)

68. Simkum, S. Investigation of Streptococcus suis outbreak in Mueang, Phetchabul Province, in 2010. In *Report of Outbreak Investigation*; Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health: Nonthaburi, Thailand, 2010. (In Thailand)

69. Kerdsin, A.; Oishi, K.; Sripakdee, S.; Boonkerd, N.; Polwichai, P.; Nakamura, S.; Uchida, R.; Sawanpanyalert, P.; Dejsirilert, S. Clonal dissemination of human isolates of *Streptococcus suis* serotype 14 in Thailand. *J. Med. Microbiol.* 2009, 58, 1508–1513. [CrossRef] 
[PubMed]

70. Kerdsin, A.; Hatrongjit, R.; Wongsurawat, T.; Jenjaroenpun, P.; Chopjitt, P.; Boueroy, P.; Fittipaldi, N.; Zheng, H.; Gottschalk, M. Genomic Characterization of *Streptococcus suis* Serotype 24 Clonal Complex 221/234 From Human Patients. *Front. Microbiol.* 2021, 12, 812436. [CrossRef] [PubMed]

71. Kerdsin, A.; Takeuchi, D.; Akeda, Y.; Nakamura, S.; Gottschalk, M.; Oishi, K. Genomic differences between sequence types 1 and 104 of *Streptococcus suis* Serotype 2. *PeerJ* 2022, 10, e14144. [CrossRef]

72. Takeuchi, D.; Akeda, Y.; Nakayama, T.; Kerdsin, A.; Sano, Y.; Kanda, T.; Hamada, S.; Dejsirilert, S.; Oishi, K. The Contribution of Suilysin to the Pathogenesis of *Streptococcus suis* Meningitis. *J. Infect. Dis.* 2014, 209, 1509–1519. [CrossRef]

73. Kerdsin, A.; Takeuchi, D.; Nuangmek, A.; Akeda, Y.; Gottschalk, M.; Oishi, K. Genotypic Comparison between *Streptococcus suis* Isolated from Pigs and Humans in Thailand. *Pathogens* 2020, 9, 50. [CrossRef]

74. Maneerat, K.; Yongkiettrakul, S.; Kramomtong, I.; Tongtawe, P.; Luangsuk, P.; Chaicumpa, W.; Gottschalk, M.; Srimanote, P. Virulence Genes and Genetic Diversity of *Streptococcus suis* Serotype 2 Isolates from Thailand. *Transbound. Emerg. Dis.* 2013, 60 (Suppl. 2), 69–79. [CrossRef]

75. Tharavichitkul, P.; Wongsawan, K.; Takenami, N.; Pruksakorn, S.; Fongcom, A.; Gottschalk, M.; Kanthawa, B.; Supajatura, V.; Takai, S. Correlation between PFGE Groups and *mrp/epf/sly* Genotypes of Human *Streptococcus suis* Serotype 2 in Northern Thailand. *J. Pathog.* 2014, 2014, 350416. [PubMed]

76. Bamphegsins, N.; Chopjitt, P.; Hatrongjit, R.; Boueroy, P.; Fittipaldi, N.; Gottschalk, M.; Kerdsin, A. Non-Penicillin-Susceptible *Streptococcus suis* Isolated from Humans. *Pathogens* 2021, 10, 1178. [CrossRef] [PubMed]

77. Vilaichone, R.K.; Mahachai, V.; Nonthapisud, P. *Streptococcus suis* peritonitis: Case report. *J. Med. Assoc. Thai.* 2000, 83, 1274–1277. [CrossRef]

78. Bojarska, A.; Molska, E.; Janas, K.; Skoczynska, A.; Stefanik, E.; Hryniewicz, W.; Sadowy, E. *Streptococcus suis* in invasive human infections in Poland: Clonality and determinants of virulence and antimicrobial resistance. *Eur. J. Clin. Microbiol. Infect. Dis.* 2016, 35, 917–925. [CrossRef] [PubMed]

79. Huo, N.T.; Chieu, T.T.; Nghia, H.D.; Mai, N.T.; Anh, P.H.; Wolbers, M.; Baker, S.; Campbell, J.I.; Chau, N.V.; Hien, T.T.; et al. The antimicrobial resistance patterns and associated determinants in *Streptococcus suis* isolated from humans in southern Vietnam, 1997–2008. *BMJ Infect. Dis.* 2011, 11, 6. [CrossRef] [PubMed]

80. Marie, J.; Morvan, H.; Berthelot-Heurault, E.; Sanders, P.; Kempf, I.; Gautier-Bouchardon, A.V.; Jouy, E.; Kobisch, M. Antimicrobial susceptibility of *Streptococcus suis* isolated from swine in France and from humans in different countries between 1996 and 2000. *J. Antimicrob. Chemother.* 2002, 50, 201–209. [CrossRef] [PubMed]

81. Ye, C.; Bai, X.; Zhang, J.; Jing, H.; Zheng, H.; Du, H.; Cui, Z.; Zhang, S.; Jin, D.; Xu, Y.; et al. Spread of *Streptococcus suis* sequence type 7, China. *Emerg. Infect. Dis.* 2008, 14, 787–791. [CrossRef]

82. Chang, B.; Wada, A.; Ikebe, T.; Ohnishi, M.; Mita, K.; Endo, M.; Matsu, H.; Asatuma, Y.; Kuramoto, S.; Sekiguchi, H.; et al. Characteristics of *Streptococcus suis* isolated from patients in Japan. *Jpn. J. Infect. Dis.* 2006, 59, 397–399. [CrossRef]

83. Chu, Y.W.; Cheung, T.K.; Chu, M.Y.; Tsang, V.Y.; Fung, J.T.; Kam, K.M.; Lo, J.Y. Resistance to tetracycline, erythromycin and clindamycin in *Streptococcus suis* serotype 2 in Hong Kong. *Int. J. Antimicrob. Agents* 2009, 34, 181–182. [CrossRef] [PubMed]

84. Nga, T.V.T.; Nghia, H.D.T.; Tu, L.T.P.; Diep, T.S.; Mai, N.T.H.; Chau, T.T.H.; Sinh, D.X.; Phu, N.H.; Chau, N.V.V.; Campbell, J.; et al. Real-time PCR for detection of *Streptococcus suis* serotype 2 in cerebrospinal fluid of human patients with meningitis. *Diagn. Microbiol. Infect. Dis.* 2011, 70, 461–467. [CrossRef] [PubMed]

85. Nakayama, T.; Zhao, J.; Takeuchi, D.; Kerdsin, A.; Chiranairadul, P.; Areearatana, P.; Loethhong, P.; Pienpringam, A.; Akeda, Y.; Oishi, K. Colloidal gold-based immunochromatographic strip test compromising optimised combinations of anti- S. suis capsular polysaccharide polyclonal antibodies for detection of *Streptococcus suis*. *Biosens. Bioelectron.* 2014, 60, 175–179. [CrossRef] [PubMed]

86. Zhang, X.; Wu, Z.; Wang, K. Diagnosis of *Streptococcus suis* Meningoencephalitis with metagenomic next-generation sequencing of the cerebrospinal fluid: A case report with literature review. *BMJ Infect. Dis.* 2020, 20, 884. [CrossRef] [PubMed]
87. Thu, I.; Tragoolpua, K.; Intorasoot, S.; Anukool, U.; Khamnoi, P.; Kerdsin, A.; Tharinjaroen, C.S. Direct detection of *Streptococcus suis* from cerebrospinal fluid, positive hemoculture, and simultaneous differentiation of serotypes 1, 1/2, 2, and 14 within single reaction. *Pathogens* 2021, 10, 996. [CrossRef] [PubMed]

88. Lun, Z.-R.; Wang, Q.-P.; Chen, X.-G.; Li, A.-X.; Zhu, X.-Q. *Streptococcus suis*: An emerging zoonotic pathogen. *Lancet Infect. Dis.* 2007, 7, 201–209. [CrossRef]