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Symposium voor Dierziekten

23/09/2021

Streptococcus suis: an overview, virulence, zoonotic potential and antibiotic resistance

Nadine Botteldoorn & Caroline Bonckaert

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Outline

- Who is *Streptococcus suis*?
- Pathogenicity in swine
- Disease in swine
- Pathogenicity in human
- Zoonotic disease
- Bacteriology
- Prevalence
- Antibiotic resistance
- Prevention
- Take home message

Who is *Streptococcus suis*?

Gram positive bacterium

Facultative anaerobic bacterium

Facultative pathogenic character

Obligate symbiotic

- Tonsils
- Upper respiratory tract
- Digestive system (intestines)
- Genital system (vagina)



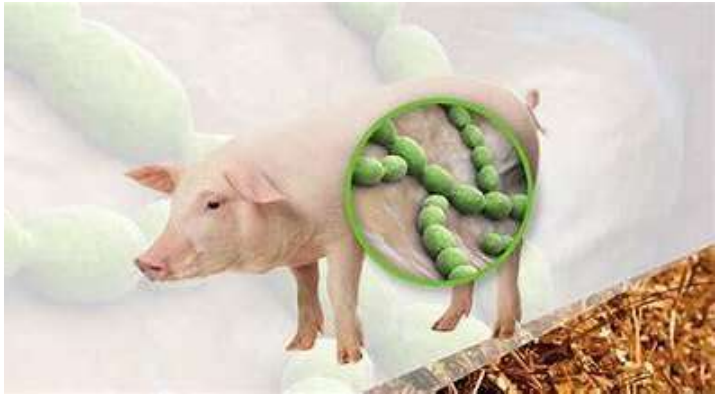



Who is *Streptococcus suis*?

Many different serotypes

Differences in virulence and pathogenicity

- Virulence markers
- Virulence associated factors
  - Surface/secreted elements
  - Protease enzymes
  - Transcription factors/regulatory systems
  - Transporters/secretion systems



Capsular polysaccharide

Extracellular factor

Muramidase-released protein

Suilysin

Pathogenicity in swine

Carrier animals

Tonsils

Digestive tract

Genital tract

Transmission

Birth

Nose-nose contact

Droplets

Flies

Death animals

Faeces

Bacteria-related

Virulence

Animal-related

Stress

Age

Pathogenicity in swine

Dissemination

Nose

Lymph nodes

Predisposing factors

Ammonia

Immunosuppressive viruses

Immunosuppressive bacteria (nose)

Blood (**septicemia**) → Spread throughout the body

Wounds

Castration

Iron injection

Teeth clipping

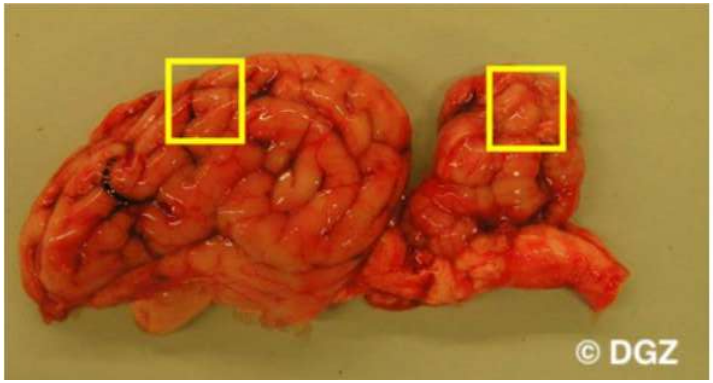
Tail docking

Rough floors

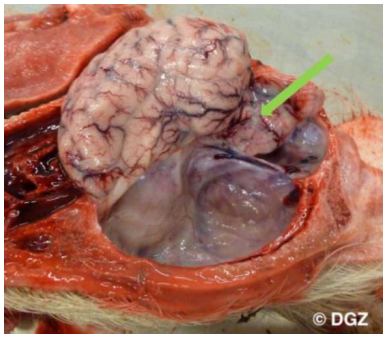
Disease in swine

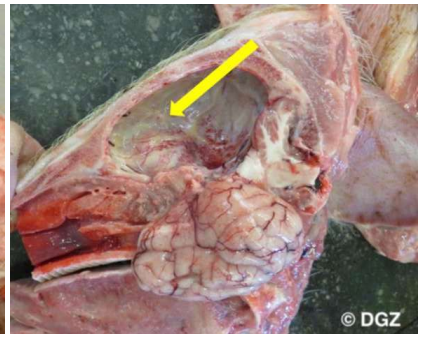
Suckling piglets

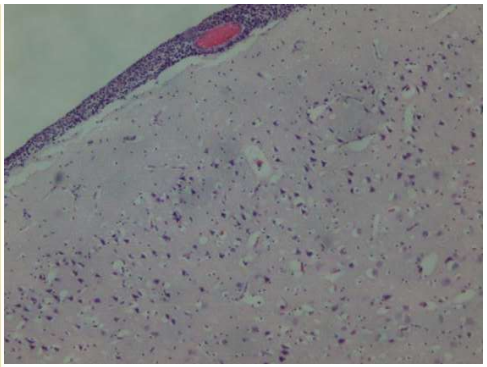
Weaned piglets

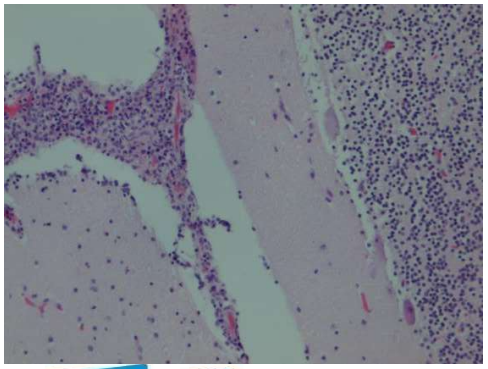


Fattening pigs









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Zoonotic disease

Oral transmission

Uncooked or raw meat

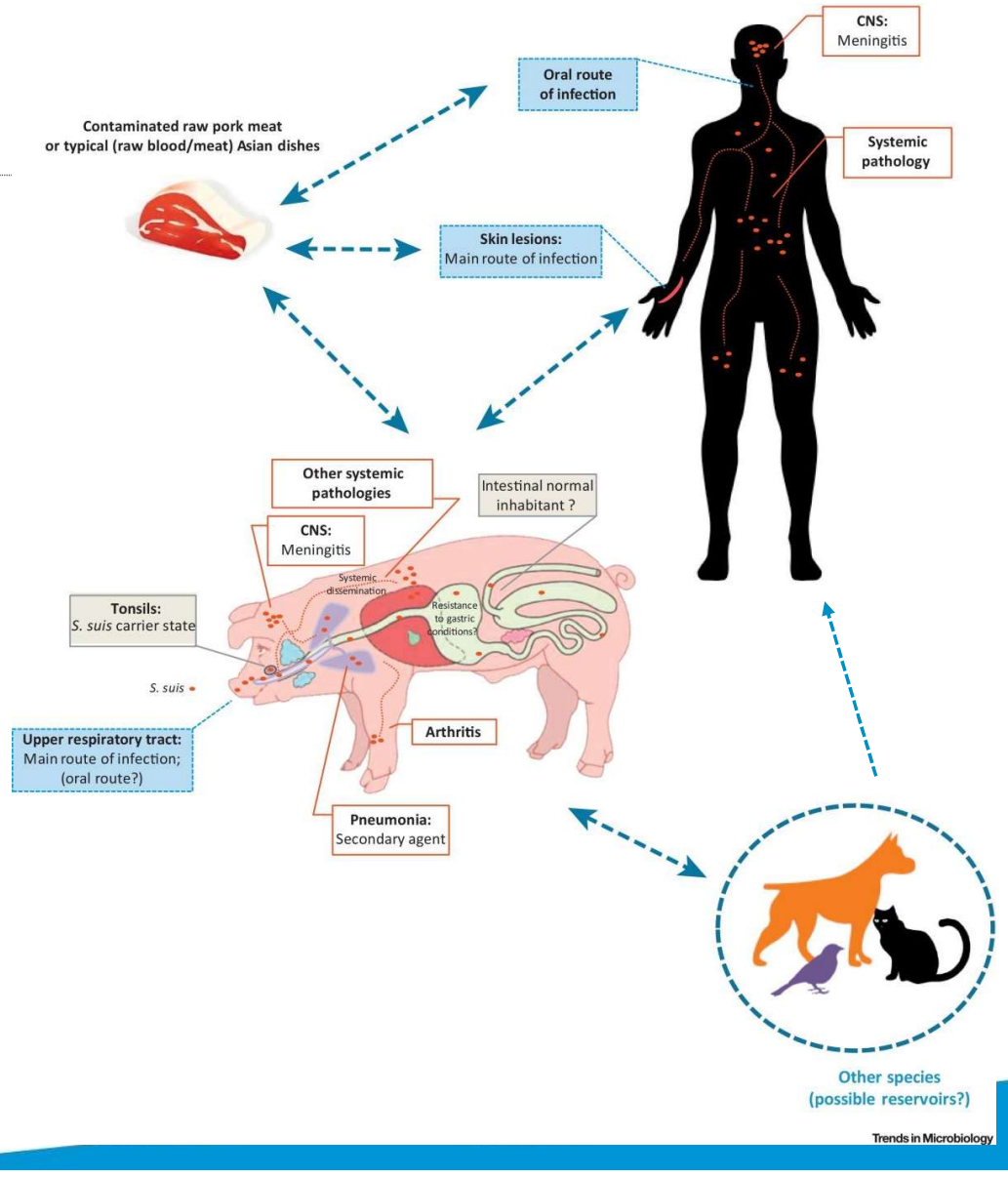
Skin lesions

Farmers
Pet owners
Butchers
Veterinarians

Septicemia →

Meningitis
Pneumonia
Endocarditis
Polyarthritis

Hearing loss



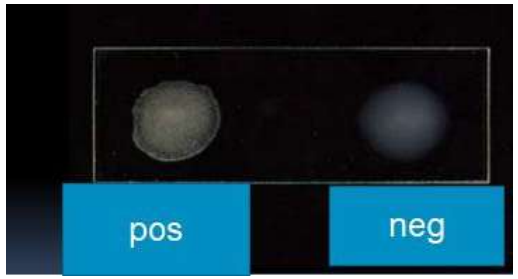
Bacteriology

Aerobic culture of the organs like spleen, brain, joint

Bloodagar

Identification with the maldi tof

Serotyping with slide agglutination for the most important serotypes 1,2,3,4,7,8,en 9



		Aërobe standaard cultuur		Typering
Monsterinfo	**Materiaal**	**Resultaat**		**Resultaat**
(007) jejunum GESPEEND BIG	Jejunum inhoud (swab 1)	Escherichia coli	POS+++	
		Haem. Escherichia coli (*1)	POS+	
(013) hersenen GESPEEND BIG	Hersenen (1)	Haem. Escherichia coli	POS+	
		Streptococcus suis	POS+++	serotype 9
	Hersenen (2)	Escherichia coli	POS++	
		Haem. Escherichia coli	POS++	
		Streptococcus suis	POS+++	serotype 9
	Hersenen (3)	Escherichia coli	POS+	
		Haem. Escherichia coli	POS+	
		Streptococcus suis (*2)	POS+++	serotype 9

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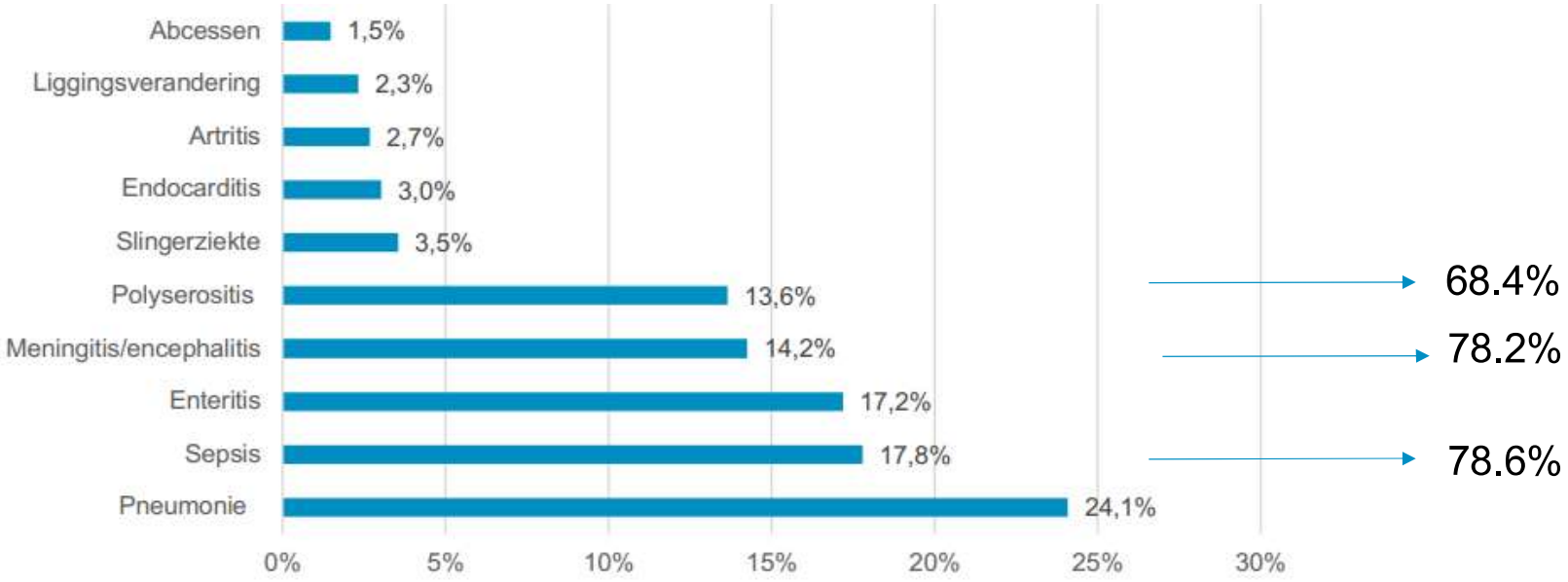
Numbers out of necropsy DGZ-2020



The ten most common causes of injury or death for weaned piglets and fattening pigs to 40 kg (data 2020-necropsy).

Distribution of *Streptococcus suis* serotypes causing illness

Pigs

Table 1 Worldwide distribution of serotypes for reported clinical *S. suis* cases of infection in pigs by country from 1 January 2002 to 31 December 2013

Country	Clinical cases	Predominant serotypes[a] (frequency in %)			Reference
Worldwide	4711	2 (27.9%)	9 (19.4%)	3 (15.9%)	
North America	3162 (67.1%)	2 (24.3%)	3 (21.0%)	1/2 (13.0%)	
Canada	3 065	2	3	1/2	25, 29
United States	97	3	2	7	55
South America	125 (2.7%)	2 (57.6%)	1/2 (9.6%)	14 (8.8%)	
Brazil	125	2	1/2	14	56,57
Asia	659 (14.0%)	2 (44.2%)	3 (12.4%)	4 (5.6%)	
Mainland China	639	2	3	4	30,58–60
South Korea	20	3	4	2, 8, 22	61
Europe	765 (16.2%)	9 (61.0%)	2 (18.4%)	7 (6.7%)	
Netherlands	99	9	2	7	62
Spain	666	9	2	7	63–65

[a] Only the three most predominant serotypes, which were identified by co-agglutination (or an equivalent method using reference antisera), are shown in this table.

Intercontinental differences in pathogenic serotypes in pigs

Europe serotype 9 most important
Asia and America 2 most important serotype

In humans serotype 2 most important

Human

OPEN

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www.nature.com/emi

REVIEW

***Streptococcus suis*, an important pig pathogen and emerging zoonotic agent—an update on the worldwide distribution based on serotyping and sequence typing**

Guillaume Goyette-Desjardins[1,*], Jean-Philippe Auger[1,*], Jianguo Xu[2], Mariela Segura[1] and Marcelo Gottschalk[1]

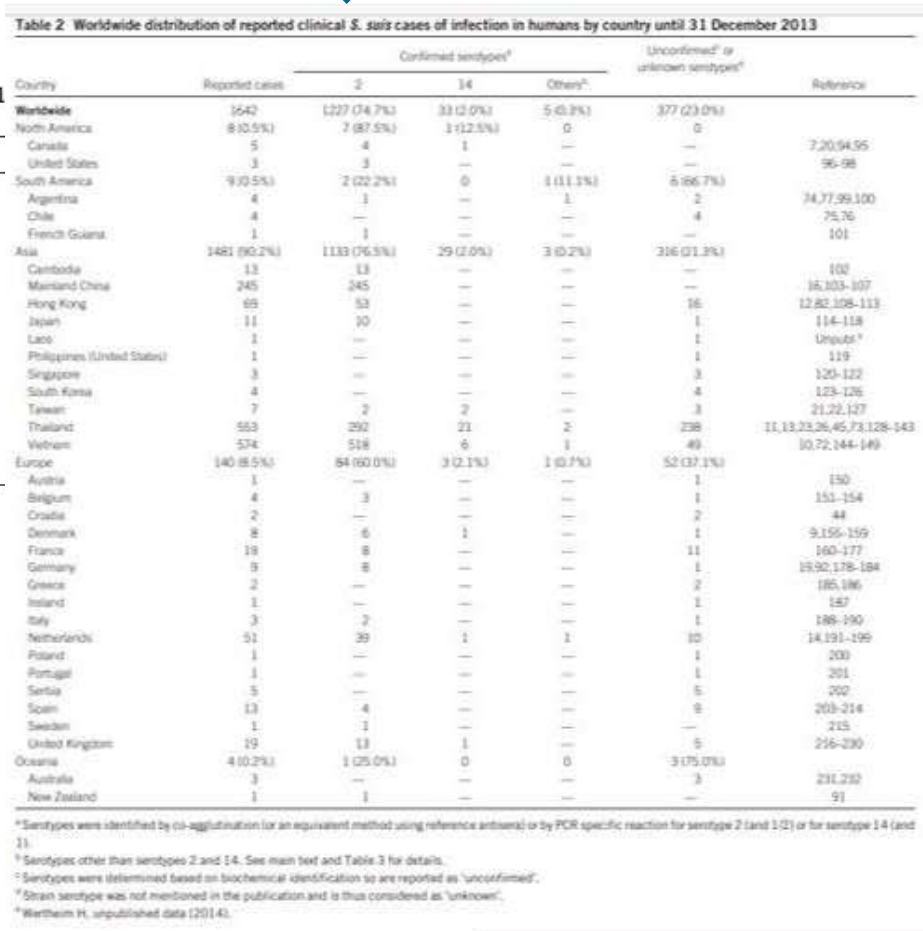


Table 2 Worldwide distribution of reported clinical *S. suis* cases of infection in humans by country until 31 December 2013

Country	Reported cases	Confirmed serotypes[a]			Unconfirmed[c] or unknown serotypes[d]	Reference
		2	14	Others[b]		
Worldwide	1642	1227 (74.7%)	33 (2.0%)	5 (0.3%)	377 (23.0%)	
North America	8 (0.5%)	7 (87.5%)	1 (12.5%)	0	0	
Canada	5	4	1	—	—	7,20,94,95
United States	3	3	—	—	—	96–98
South America	9 (0.5%)	2 (22.2%)	0	1 (11.1%)	6 (66.7%)	
Argentina	4	1	—	1	2	74,77,99,100
Chile	4	—	—	—	4	75,76
French Guiana	1	1	—	—	—	101
Asia	1481 (90.2%)	1133 (76.5%)	29 (2.0%)	3 (0.2%)	316 (21.3%)	
Cambodia	13	13	—	—	—	102
Mainland China	245	245	—	—	—	16,103–107
Hong Kong	69	53	—	—	16	12,82,108–113
Japan	11	10	—	—	1	114–118
Laos	1	—	—	—	1	Unpubl.[e]
Philippines (United States)	1	—	—	—	1	119
Singapore	3	—	—	—	3	120–122
South Korea	4	—	—	—	4	123–126
Taiwan	7	2	2	—	3	21,22,127
Thailand	563	292	21	2	238	11,13,23,26,45,73,128–143
Vietnam	574	518	6	1	49	10,72,144–149
Europe	140 (8.5%)	84 (60.0%)	3 (2.1%)	1 (0.7%)	52 (37.1%)	
Austria	1	—	—	—	1	150
Belgium	4	3	—	—	1	151–154
Croatia	2	—	—	—	2	44
Denmark	8	6	1	—	1	9,155–159
France	19	8	—	—	11	160–177
Germany	9	8	—	—	1	19,92,178–184
Greece	2	—	—	—	2	185,186
Ireland	1	—	—	—	1	187
Italy	3	2	—	—	1	188–190
Netherlands	51	39	1	1	10	14,191–199
Poland	1	—	—	—	1	200
Portugal	1	—	—	—	1	201
Serbia	5	—	—	—	5	202
Spain	13	4	—	—	9	203–214
Sweden	1	1	—	—	—	215
United Kingdom	19	13	1	—	5	216–230
Oceania	4 (0.2%)	1 (25.0%)	0	0	3 (75.0%)	
Australia	3	—	—	—	3	231,232
New Zealand	1	1	—	—	—	91

[a] Serotypes were identified by co-agglutination (or an equivalent method using reference antisera) or by PCR specific reaction for serotype 2 (and 1/2) or for serotype 14 (and 1).
[b] Serotypes other than serotypes 2 and 14. See main text and Table 3 for details.
[c] Serotypes were determined based on biochemical identification so are reported as 'unconfirmed'.
[d] Strain serotype was not mentioned in the publication and is thus considered as 'unknown'.
[e] Wertheim H, unpublished data (2014).

Human cases in Belgium

No reference centre in Belgium or on European level

Hospital in Liege

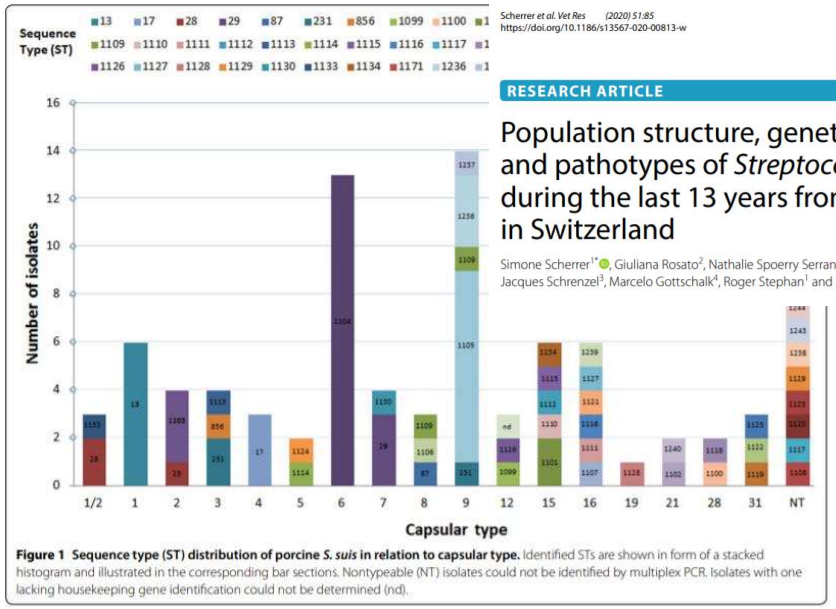
From 2016 – 2020 no bloodstream infections with *Streptococcus suis*

Hospital in Ieper

From 2012 –2020 4 patients with a positive bloodculture

- 1 person with dental abscesses: endocarditis
- 1 pig farmer with splenectomy: fever with unclear focus
- 1 person: unclear focus
- 1 person: unknown

Genetic diversity within *Streptococcus suis*



Scherrer et al. Vet Res (2020) 51:85
https://doi.org/10.1186/s13567-020-00813-w

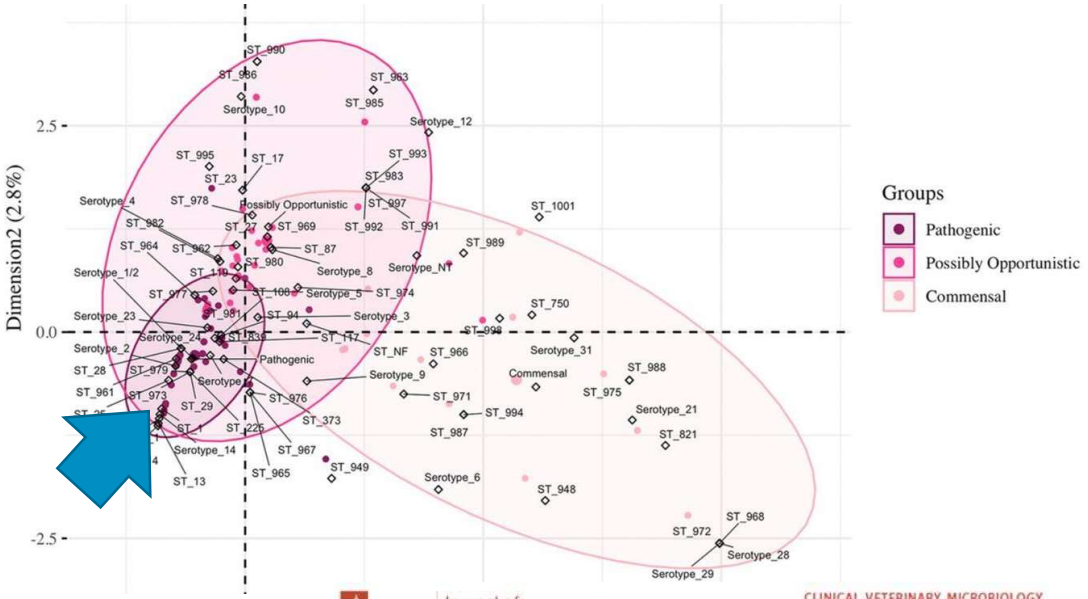
VETERINARY RESEARCH

RESEARCH ARTICLE Open Access

Population structure, genetic diversity and pathotypes of *Streptococcus suis* isolated during the last 13 years from diseased pigs in Switzerland

Simone Scherrer[1*], Giuliana Rosato[2], Nathalie Spoerry Serrano[1], Marc J. A. Stevens[1], Fenja Rademacher[1], Jacques Schrenzel[3], Marcelo Gottschalk[4], Roger Stephan[1] and Sophie Peterhans[1]

Figure 1 Sequence type (ST) distribution of porcine *S. suis* in relation to capsular type. Identified STs are shown in form of a stacked histogram and illustrated in the corresponding bar sections. Nontypeable (NT) isolates could not be identified by multiplex PCR. Isolates with one lacking housekeeping gene identification could not be determined (nd).



Most pathogenic group

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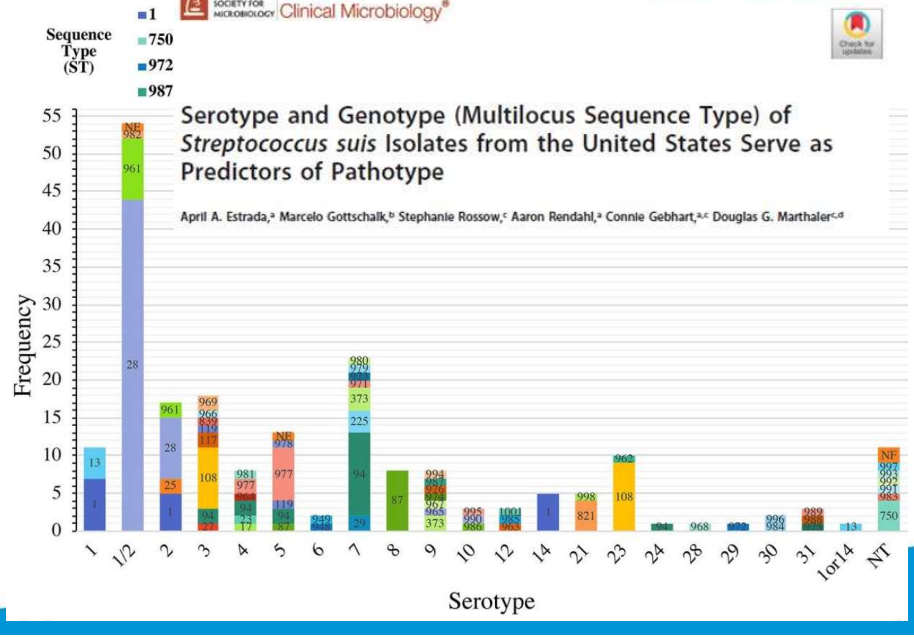
CLINICAL VETERINARY MICROBIOLOGY



Serotype and Genotype (Multilocus Sequence Type) of *Streptococcus suis* Isolates from the United States Serve as Predictors of Pathotype

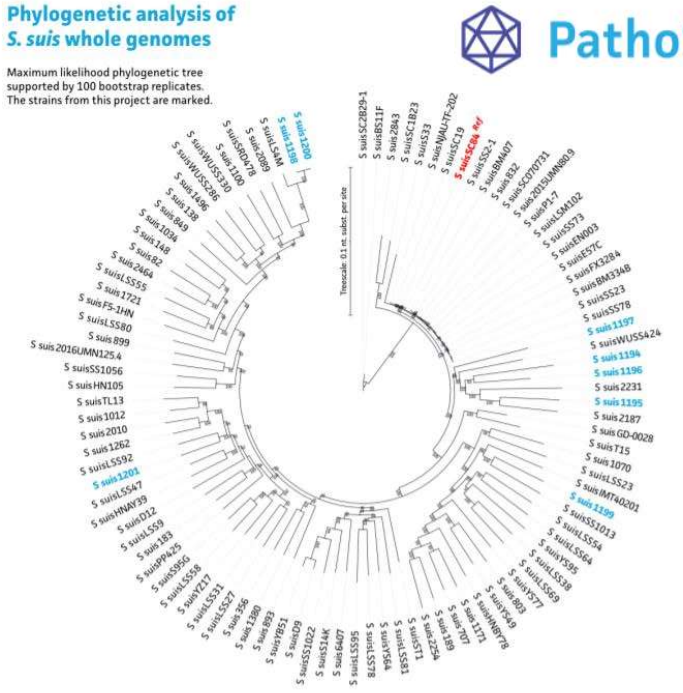
April A. Estrada,[a] Marcelo Gottschalk,[b] Stephanie Rossow,[c] Aaron Rendahl,[a] Connie Gebhart,[a,c] Douglas G. Marthaler[c,d]

Within a serotype a big genetic variation and also difference in pathogenicity

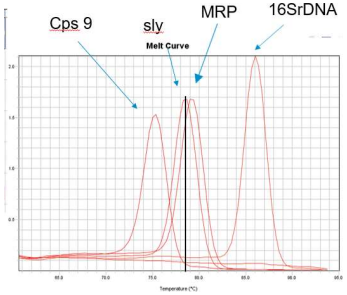
Own study with WGS

Tonsil swabs and faecal swabs of piglets just after weaning : The bacteriology gives *Streptococcus suis* NT

By WGS : Very heterogenous strains



Figuur 1. Fylogenetische analyse van S. suis genomen. *De legende toont de genetische afstand a he aantal nucleotide substituties per site. De stamen van deze analyse, 1-0001194-1200 zijn aangeduid in het blauw; de ncbi referentiestam (S. suis CS84) in het rood.*



Virulence typing

	1194	1195	1196	1197	1198	1199	1200	1201
VF (totaal)	*9*	*9*	*9*	*9*	*18*	*18*	*18*	*16*
fbp54	99.94	99.76	99.70	99.94	99.82	99.94	99.76	99.94
cbpD	.	.	.	.	99.79	.	99.79	100.0
plr/gapA (Spy)	.	.	99.81	.	.	.	.	.
plr/gapA (Sag)	.	.	.	.	99.80	99.80	99.80	99.80
plr/gapA (Spn)	97.31	97.31	97.04	95.56	.	.	.	.
ssp-5	.	.	.	99.82	.	99.90	.	.
SSU98_0978	99.98	99.70	99.76	99.92	99.82	99.82	99.82	99.96
zmpC	.	.	.	.	99.34	.	99.34	.
hylA	.	.	.	.	99.55	.	99.55	.
mrp	.	.	.	.	90.20	.	90.20	.
sly	.	.	.	.	100.00	.	100.00	.
Cps2A	.	.	.	.	99.93	.	99.93	100.00
Cps2C	.	.	.	.	95.98	99.86	95.83	95.83
Cps2E	.	.	.	.	.	99.42	.	.
Cps2D	.	.	.	.	98.63	.	98.50	95.77
str1083	99.38	95.06	100.0	.	95.68	95.68	95.68	95.68
STER_1222	.	100.0	100.0	.	.	100.0	.	.
SSU05_0577	.	.	.	.	.	99.72	.	.
SSU05_0578	.	.	.	.	.	99.90	.	100.0
SSU05_0579	.	.	.	.	.	99.91	.	.
SSU05_0580	.	.	.	.	.	99.23	.	99.69
SSU05_0581	.	.	.	.	.	100.00	.	.
SSU98_0580	.	.	.	.	.	100.00	.	.
STER_1224	.	99.43	.	.	.	.	.	.
RmlC	96.30	96.13	.	96.13	96.30	96.13	96.30	96.30
RmlA	99.77	.	99.77	99.66	99.77	99.77	99.77	99.77
RmlB	100.0	.	.	100.0	100.0	.	100.0	100.0
tig/ropA (Hun)	99.69	99.61	.	99.69	99.69	99.69	99.69	99.69
tig/ropA (TIG)	.	.	86.37	.	.	.	.	.
Ofs	.	.	.	.	89.96	.	89.96	89.82
SSU98_1513	100.0	100.0	99.77	99.92	100.0	100.0	100.0	100.0

MLST sequence typing

	Closest ST	*aroA*	*cpn60*	*dpr*	*gki*	*mutS*	*recA*	*thrA*
1-0001194	*NA*	**250**	353	200	308	166	206	**123**
1-0001195	*NA*	**146**	208	29	344	320	274	**123**
1-0001196	*NA*	**166**	**106**	211	199	283	126	123
1-0001197	1591	**250**	290	143	262	208	186	180
1-0001198	43	35	36	27	13	37	28	29
1-0001199	*NA*	224	420	131	95	348	142	179
1-0001200	43	35	36	27	13	37	28	29
1-0001201	1280	33	12	293	19	30	26	12

High number of SNPs within allele; NA = too many Closest ST

NA = No ST could be concluded from the obtained MLST profile, due to highly divergent alleles.

Antimicrobial resistance

	1194	1195	1196	1197	1198	1199	1200	1201
AMR genen (totaal)	6	2	4	6	2	3	2	7
*(**Strep**)ant6-Ia*	100.0	.	.	100.0	.	.	.	100.0
*(**Ami/Kan**)aph(3'')-III*	.	.	.	100.0	.	.	.	99.87
*(**Ami/Kan**)spw*	99.88	.	.	99.88	.	.	.	99.88
*(**MLS**)erm(B)*	100.0	99.87	100.0	100.0	100.0	100.0	100.0	100.0
*(**Lin**)lnu((B)*	100.0	.	.	.	.	.	.	.
*(**Tet**)tet(O/W/32/O)*	99.90	99.95	99.90	99.69	99.95	99.79	99.95	99.95
*(**Tet**)tetM*	.	.	.	.	.	.	.	99.84
*(**MDR**)lsae*	100.0	.	.	.	.	.	.	.
*(**Plasmid**)pA852*	.	.	94.15	94.15	.	.	.	.
*(**Plasmid**)pBM407*	.	.	100.0	.	.	99.93	.	.
*(**Plasmid**)DOp1*	.	.	.	.	.	.	.	100.0

Afkortingen: Strep: Streptomycin; Ami/Kan: Amikacin/Kanamicin; MLS: Macrolide, lincosamide and streptogramin group; Lin: Lincosamide; Tet: Tetracycline; MDR: Multi-Drug-Resistance

Fight against antibiotic resistance at National level

21/07/2016 New legislation on veterinary medicinal products

Wetgeving diergeneesmiddelen

Koninklijk besluit van 21/07/2016 (PDF) betreffende de voorwaarden voor het gebruik van geneesmiddelen door de dierenartsen en door de verantwoordelijken van de dieren
(Nummer NUMAC - 2016024152 - voor de gecoördineerde wetgeving)

Het K.B. van 21/07/2016 betreffende de voorwaarden voor het gebruik van geneesmiddelen door de dierenartsen en door de verantwoordelijken van de dieren werd gepubliceerd in het Belgisch Staatsblad op 29/07/2016. Het treedt in voege op 08/08/2016.

27/02/2017 Registration of the antibiotics in Sanitel -MED

Importance of the determination of the antimicrobial resistance for a responsible antibiotic use

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E-formularium

Keuze van het antibioticum/chemotherapeuticum. (Klik op de naam om de bijsluiter te raadplegen)

Eerste keuze(s)

procaïne benzylpenicilline

Tweede keuze(s)

trimethoprim + sulfonamiden

amoxicilline

ampicilline

procaïne benzylpenicilline + neomycine

Derde keuze(s)

lincomycine

oxytetracycline

cefquinome

ceftiofur

Streptokokkensepticemie

Indicaties en opmerkingen

Septicemie bij biggen wordt hoofdzakelijk veroorzaakt door *Streptococcus suis*, maar ook andere streptokokken kunnen dergelijke letsels veroorzaken. Streptokokken zijn bewoners van de neus en tonsillen. Onder invloed van stressfactoren kan de kiem een sepsis veroorzaken eventueel in combinatie met aantasting van organen of serosae.

Preventief moet **in eerste instantie aandacht** besteed worden **aan het vermijden van stressfactoren, klimaat, hokbezetting, enz.** De stressinvloeden in de moderne varkenshouderij (speenleeftijd, hergroeperen, ...) zijn echter dikwijls van die aard dat bij spenen van biggen preventief gemedicineerd wordt om uitbraken van streptokokken te voorkomen.

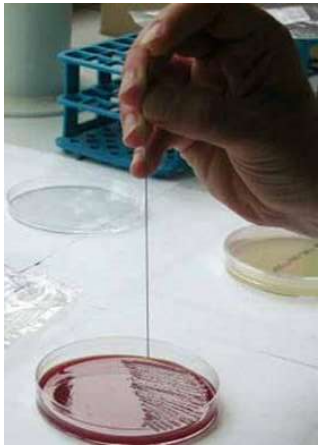
Voor zieke dieren is **onmiddellijk ingrijpen met antibacteriële middelen** noodzakelijk. Daarbij worden best ook de naburige dieren behandeld omdat bij verhoogde infectiedruk de andere biggen een groot risico op kliniek lopen.

Omschrijving LIMS	Kleurcode	Klasse
AB Penicilline [A]	Geel	Penicillines
AB Amoxycilline [B]	Oranje	Penicillines
AB Ceftiofur [C]	Rood	3e generatie cefalosporines
AB Cefoxitine		cephamycine
AB Oxacilline		Penicillines
AB Cefquinome [C]	Rood	4e generatie cefalosporines
AB Cefalexine [A]	Geel	1e generatie cefalosporines
AB Tetracycline [B]	Oranje	Tetracyclines
AB Doxycycline [B]	Oranje	Tetracyclines
AB Kanamycine [B]	Oranje	Aminoglycosides
AB Sulfa-trimethoprim [A]	Geel	Methoprim + sulfonamiden
AB Florfenicol [A]	Geel	Chloramphenicolen
AB Lincomycine [B]	Oranje	Lincosamides
AB Erythromycine [B]	Oranje	Macroliden
AB Tylosine [B]	Oranje	Macroliden
AB Enrofloxacine [C]	Rood	2e generatie fluoroquinolones

Panel in the laboratory

Antibiogram

Growth on Mueller Hinton agar with sheepblood
Panel specific for Gram + bacteria



McFarland 0,5

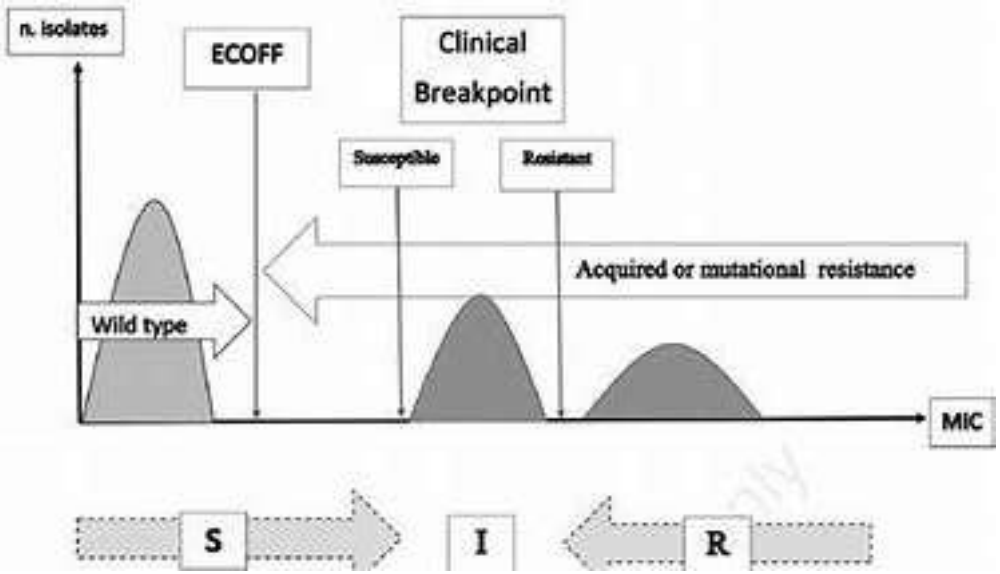
Sirscan --→ lims

BELAC

DGZ
SAMEN VOOR GEZONDE DIEREN

Breakpoints (R/I/S)

nr	GRAMPOSITIEF	Lading
1	Penicilline	10 UI
2	Amoxycilline	25 µg
3	Cefoxitine (niet op BPV)	30 µg
4	Oxacilline (niet op BPV)	5µg
5	Cefalexine	30 µg
6	Ceftiofur	30 µg
7	Cefquinome	30 µg
8	Tetracycline	30 µg
9	Doxycycline	30 µg
10	Enrofloxacine	5 µg
11	Kanamycine	30 µg
12	Tri – sulfa	1.25 + 23.75 µg
13	Florfenicol	30 µg
14	Lincomycine	15 µg
15	Erythromycine	15 µg
16	Tylosine	30 µg



A la suite des recommandations du Comité d'Experts de la Standardisation biologique de l'OMS (rapports techniques n° 610, 1977), la Société Française de Microbiologie a créé un Comité de l'Antibiogramme (CA-SFM) chargé de déterminer les valeurs critiques qui délimitent les catégories cliniques (antérieurement catégories thérapeutiques) et de proposer un guide pour la détermination de la sensibilité des bactéries aux antibiotiques en association avec l'EUCAST. Les valeurs critiques définies pour les concentrations et les diamètres des zones d'inhibition, ainsi que les

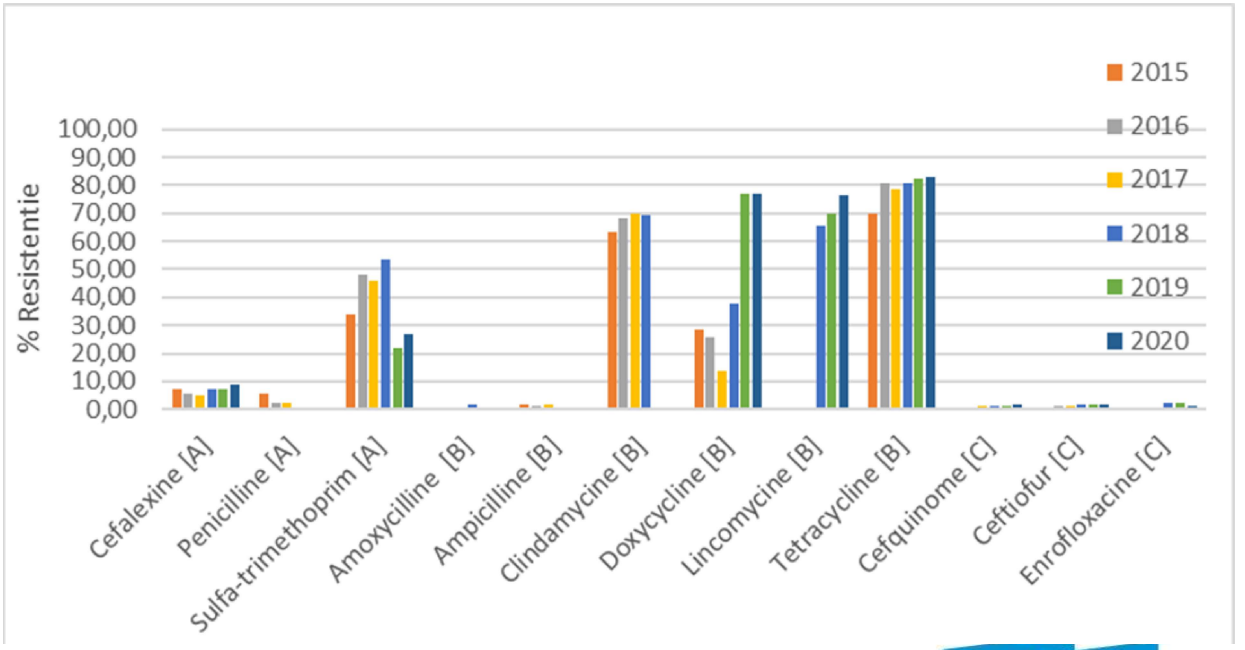
Results and trends on antimicrobial resistance

Penicilline

Sulfa-trimethoprim, Lincomycine and Tetracyclines

Cefquinome, Ceftiofur and Enrofloxacine

Year	2015	2016	2017	2018	2019	2020
Number	241	296	400	511	572	647



Prevention

Pigs

Biosecurity

Autovaccines

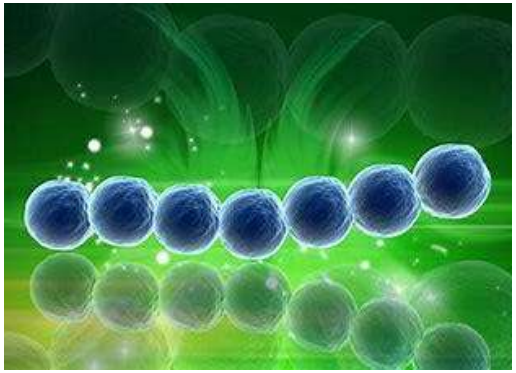
Hygiene and management (ventilation, animal density, avoiding stress)

Human

Awareness (traveling, hygiene…)

Conclusion and take home message !!

- *Streptococcus suis :* important pig pathogen with big economic impact
- *Streptococcus suis* is a very diverse species with a lot of serotypes, pathotypes
- The genes resposible for virulence are - to date - not clear (virulence-associated genes)
- In European pig population serotype 9 very important; in other countries (NA, Asian) serotype 2
- The zoonotic impact is low in EU, in Asian countries higher
- Antimicrobial resistance: penicilline is still the first antibiotic to be used
- Data collection in hospitals is needed!



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Questions?

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