CHARITÉ
UNIVERSITÄTSMEDIZIN BERLIN

Invasive infections and sepsis caused by Group A streptococci - A rising threat?

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Agenda

1. Introduction to GAS
2. Pathogenesis
3. Clinical manifestations
4. Epidemiology
5. Outlook

Case

[redacted]

F * [redacted] 2013 (12 [J])

cm* 6. ITS-Tag 11.08.2025 11:03 - 16.08.2025 22:45

Kopfumfang 20 kg* 120 cm* [redacted]

CAVE | Isolation | bisher keine Allergien dokumentiert | Monitoringplatz H | Stationsübersicht...

Tageskurve

Akte geschlossen!

11.08.2025 | 06:00 07:00 08:00 09:00 10:00 11:00 12:00 13:00 14:00 15:00 16:00 17:00 18:00 19:00 20:00 21:00 22:00 23:00 00:00 01:00 02:00 03:00 04:00 05:00

Vitalparameter | Beatmung | Organersatz | ECLS/ECMO | Kreislaufverfahren | Ereign. | Glu / K | Vasoaktiva | Gesamtbilanz

Vitalparameter

Dokumentationsunterbrechung

1. SpO2 (r %	Temp 1 °C	HF 1/min		CPP mmHg
93	41	185	185	60
90	39,5	158	NIBP 158	ICPm 50
86	38	130	130	40
83	36,5	103	ABP 103	AF 30
79	35	75	75	20
2. SpO2 (li 76	Temp 2 33,5	Puls 48	Druck 2 48	ZVD 10
72	32	20	20	0

Ereignisse: BGA | BG¶ BGA | BGA | BGA | BGA | BGA | BGA | BGA | BGA | BG¶ BGA

SpO2 %: 97 | 95 | 97 | 95 | 94 | 95 | 93 | 93 | 72 | 83 | 100 | 100 | 100

Positionierung: K-mi,Rü30°,H-bew.,F-frei (Ü 1P) | K-mi,Rü30° (Ü 1P) | K-mi,Rü30° (Ü 1P) | Rü30°,H-bew.,F-frei (Ü 1P)

Assistenz: A-Rea,A-NotIntubation (Ü)

Beatmung: Evita V600/PC-BIPAP | Evita V600/VC-AC

fiO2 (%): 75,00 | 75,00 | 75,00 | 75,00 | 75,00 | 75,00 | 75,00 | 80,00 | 80,00 | 80,00 | 80,00 | 80,00 | 80,00 | 70,00 | 60,00 | 50,00 | 50,00 | 50,00 | 50,00

Organersatz

ECLS / ECMO

Ereignisse

Besuch: Mutter

Diagnostik / Maßnahmen: Sonographie | Transkranielle Duplexsonographie TCD

Isolation: MRE-Isolation Präemptiv

Temperaturmanagement: Arctic Sun

Glucose 60 .. 100 mg/dl	22	60	82	132	184	207	241	283		333	319	335	316	301	248		229	209	179	
Kalium 3,3 .. 4,6 mmol/L	5,1	2,6	2,8	3,7	3,2	2,8	3,9	3,8		3,7	3,6	4,0	3,9	3,8	3,3		3,2	4,6	3,9	

Medikamentengabe: Vasoaktiva

Epinephrin EPINEPHrin	i.v.	mg	1 1
EPINEPHrin 1 mg/50ml (¶	i.v. kont.	µg/kg/min	0,3 0,35 0,35
EPINEPHrin 10 mg/50ml ¶	i.v. kont.	µg/kg/min	0,35
Norepinephrin 1 mg/50m¶	i.v. kont.	µg/kg/min	0,35 0,35
Norepinephrin 10 mg/50r¶	i.v. kont.	µg/kg/min	0,35
Argipressin 40 IE/50ml (0,8 IE¶	i.v. kont.	I.E./h	1 2
Argipressin 40 IE/50ml (0,8 IE/¶	i.v. kont.	ml/h	3 2,7 2,4 1,8

Gesamtbilanz

Einfuhr kum.		394	820	992	1074	1155	1457	1539	1621	1733	1842	1935	2027	2120	2202	2284	2385	2466	2557	2644
Ausfuhr kum.								55	55	55	55	55	55	55	155	155	195	195	195	215
Gesamtbilanz kum.		**394**	**820**	**992**	**1074**	**1155**	**1457**	**1484**	**1566**	**1678**	**1787**	**1880**	**1972**	**2065**	**2047**	**2129**	**2190**	**2271**	**2362**	**2429**
Gesamtbilanz inkl. Blutprodukte kum.		**394**	**820**	**992**	**1129**	**1375**	**1677**	**1704**	**1786**	**1898**	**2007**	**2107**	**2216**	**2325**	**2317**	**2399**	**2460**	**2541**	**2641**	**2819**

11.08.2025		10:00	11:00	12:00	13:00	14:00	15:00	16:00	17:00	18:00	19:00	20:00	21:00	22:00	23:00	00:00	01:00	02:00	03:00	04:00	05:00	06:00	07:00	08:00	09:00
Blutgase																									
Material	..	Venous	Venous	Arterial	Arterial	Arterial	Arterial	Arterial	Arterial		arteriell	Arterial	Arterial	Arterial	Arterial	Arterial		Arterial	Venous	Arterial	ST_Not	Specified	Arterial	ST_Not ¶	Arterial
FiO2	.. %	21.0	75.0	75.0	75.0	75.0	75.0	75.0	21.0		80	80.0	80.0	80.0	80.0	70.0		60.0	50.0	50.0		50.0	50.0	50.0	45.0
pH	..	7.158	7.220	7.209	7.190	7.228	7.319	7.304	7.302		7,299	7,300	7.295	7.301	7.312	7.313		7.336	7.262	7.320		7.367	7.374	7.400	7.406
pO2	.. mmHg	26.9	40.7	118	107	80.5	71.7	67.2	67.6		74,3	80.1	81.7	84.7	106	119		122	44.7	96.0		99.5	100	113	89.5
pCO2	.. mmHg	39.3	46.0	43.5	43.0	53.0	37.7	36.6	37.8		40	39.0	40.8	39.8	39.5	36.8		33.9	48.6	41.3		39.4	40.2	38.2	40.0
sO2	.. %	35.7	59.4	97.7	95.8	92.7	92.1	91.0	90.7		92,3	93.4	94.1	94.6	96.7	97.4		97.8	72.1	96.5		97.1	97.2	98.0	98.5
HCO3	.. mmol/l	13.9	18.1	17.3	15.8	21.3	18.8	17.7	18.1		19,1	18.6	19.2	19.0	19.4	18.1		17.6	21.2	20.7		22.1	22.9	23.1	25.1
SBE	.. mmol/l	-14.5	-8.2	-10.6	-10.9	-5.1	-6.2	-7.5	-7.1		-6,3	-6.6	-6.1	-6.2	-5.7	-6.9		-7.1	-4.8	-4.4		-2.4	-1.6	-1.0	0.4
Hb	12 .. 15,4 g/dl	10.9	10.1	9.3	9.1	9.3	8.8	8.6	9.2		10,0	10.0	10.1	10.0	10.2	9.6		9.5	9.9	10.0		9.5	9.3	9.3	9.5
Hkt	36 .. 45 %	33.3	31.3	28.5	28.2	28.7	27.2	26.6	28.6		30,9	30.8	31.1	30.9	31.6	29.8		29.3	30.6	31.0		29.5	28.9	28.9	29.0
MetHb	.. %	1.4	2.1	1.3	1.9	1.8	1.8	1.6	1.5		1,6	1.5	1.4	1.0	1.4	1.4		1.5	1.6	1.6		1.4	1.4	1.4	0.4
CO_Hb	.. %	0.9	0.4	0.5	0.0	0.3	0.3	0.3	0.2		0,2	0.1	0.2	0.3	0.0	0.1		0.1	0.2	0.2		0.3	0.3	0.4	0.8
Natrium	134 .. 143 mmol/l	145	150	151	148	152	152	150	150		149	149	150	149	150	150		151	152	151		152	152	151	154
Kalium	3,3 .. 4,6 mmol/l	5.1	2.6	2.8	3.7	3.2	2.8	3.9	3.8		3,7	3.6	4.0	3.9	3.8	3.3		3.2	4.6	3.9		3.7	3.7	3.7	3.9
Calcium_ion	1,11 .. 1,25 mmol/l	1.08	1.04	1.03	1.14	1.06	1.02	1.03	1.04		1,08	1.06	1.08	1.06	1.07	1.02		1.05	1.35	1.23		1.15	1.15	1.16	1.13
Chlor	96 .. 109 mmol/l	112	116	110	121	118	120	122	120		119	122	120	121	123	123		123	121	125		122	122	122	117
Glucose	60 .. 100 mg/dl	22	60	82	132	184	207	241	263		333	319	335	316	301	248		229	209	179		114	111	93	89
Laktat	5 .. 20 mg/dl	88	110	108	80	73	74	73	75		74	69	73	70	69	61		57	63	57		47	46	42	41
Elektrolyte																									
Calcium/P	2,1 .. 2,55 mmol/l																			2.01					
Phosphor/P	0,95 .. 1,6 mmol/l									2.39										1.68					
Magnesium/P	0,66 .. 0,95 mmol/l									0.92										0.93					
Klinische Chemie																									
Kreatinin/P	0,53 .. 0,79 mg/dl		2.94							2.48										2.34					
Hst/P	15 .. 36 mg/dl		110							118										114					
Hsr/P	2,2 .. 6,4 mg/dl		8.3																						
Albumin/P	38 .. 54 g/dl		25.1							21.6										23.6					
CRP/P	.. 5 mg/l		234.2																	319.2					
PCT/S	.. 0,09 ug/l		>100.00																	>100.00					
ALT_37/P	.. 31 U/l		268																	178					
AST_37/P	16 .. 46 U/l		659							640										482					
AP_37/P	129 .. 417 U/l																			76					
GGT_37/P	5 .. 36 U/l		43																	47					
BiliT/P	.. 1,2 mg/dl		0.27																	0.79					
BiliC/P	.. 0,3 mg/dl		0.21																	0.79					
tBil	0,2 .. 1	0.1	K	0.2	0.7	0.6	0.7	0.6	0.9			1.0	0.8	0.9	1.0	1.1		1.1	1.2	1.1		1.1	1.1	1.1	0.5
CK/P	.. 167 U/l		3711							6476															
CK-MB/P	.. 24 U/l		216.7																						
CKMB%	.. %		6																						
Trop_T/P	.. 14 ng/l		105																						
LDH_37/P	120 .. 300 U/l		879							856															
NT-pro BNP HP	.. 370 ng/l		19453																						
kleines Blutbild																									
Hb/B	12 .. 15,4 g/dl		10.3																	9.7					
Hkt/B	0,355 .. 0,45 l/l		0.310																	0.280					
Ery/B	3,9 .. 5,2 /pl		3.4																	3.1					
Leuko/B	4,02 .. 11,4 /nl		3.48																	14.62					

[redacted]

F * [redacted] 2013 (12 [J]) [redacted]

cm* 6. ITS-Tag 11.08.2025 11:03 - 16.08.2025 22:45

Kopfumfang 20 kg* **perin Asphyxie -> Panhypopituitarismus**

120 cm* **Akt: sept Schock, CPR**

CAVE | Isolation | bisher keine Allergien dokumentiert | Monitoringplatz H | Stationsübersicht...

Medikationsgabe

Akte geschlossen!

11.08.2025

06:00 07:00 08:00 09:00 10:00 11:00 12:00 13:00 14:00 15:00 16:00 17:00 18:00 19:00 20:00 21:00 22:00 23:00 00:00 01:00 02:00 03:00 04:00 05:00

Vitalparameter | Visum | Blutprodukte | Vasoaktiva | Antiinfektiva

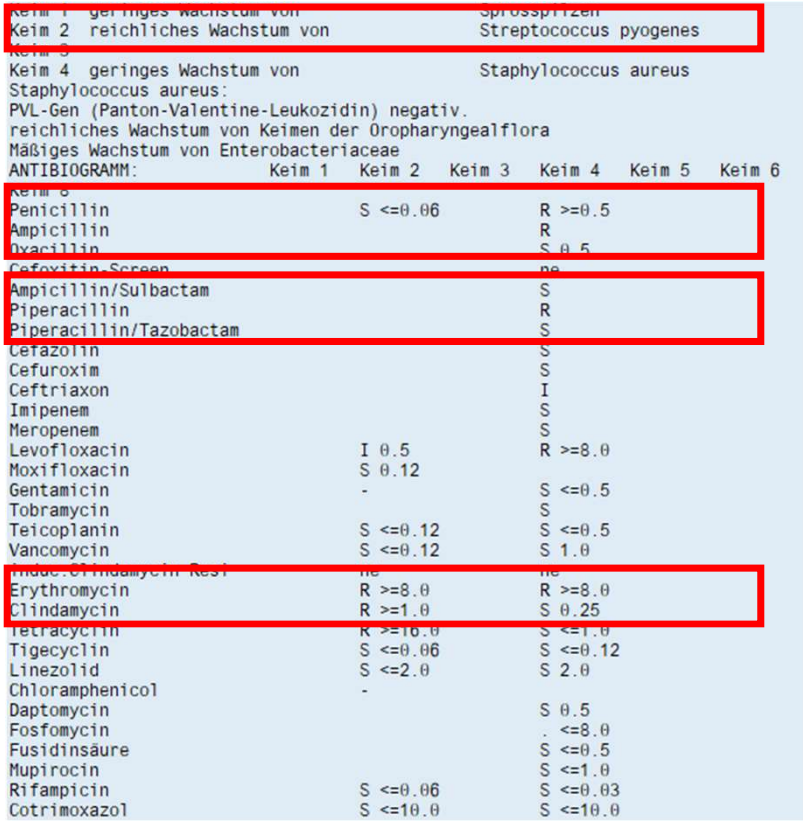
FFP	i.v.	ml/h	220
FFP	i.v.	ml/h	110
Plasmaprotein (human) Albumin huma¶	i.v.	g/h	3,333
Medikamentengabe: Vasoaktiva			
fUROsemid100 mg/50ml (2¶	i.v. kont.	mg/kg/d	
Epinephrin EPINEPHrin	i.v.	mg	1 1
EPINEPHrin 1 mg/50ml ((¶	i.v. kont.	µg/kg/min	0,3 0,35 0,35
EPINEPHrin 10 mg/50ml ¶	i.v. kont.	µg/kg/min	0,35 0,2
Milrinon 10 mg/50ml (0,2 ¶	i.v. kont.	µg/kg/min	
Norepinephrin 1 mg/50ml ¶	i.v. kont.	µg/kg/min	0,35 0,35
Norepinephrin 10 mg/50r¶	i.v. kont.	µg/kg/min	0,35
Argipressin 40 IE/50ml (0,8 IE/¶	i.v. kont.	I.E./h	1 2
Argipressin 40 IE/50ml (0,8 IE/r¶	i.v. kont.	ml/h	3 2,7 2,4 1,8
Medikamentengabe: Antiinfektiva			
Meropenem päd. 500 mg/25ml (20r¶	i.v.	mg/h	800 mg 800 mg 200 200
Vancomycin päd. ZVK 500 mg/50m¶	i.v.	mg/h	300 X 300 RG
Vancomycin päd. ZVK 500 mg/50ml (¶	i.v.	mg	600
Ambisome päd. 50 mg/25ml (2 mg/ ¶	i.v.	mg/h	60 mg
Medikamentengabe: i.m. / s.c. / sonstige			
Kalium-Ion Kalium-Ion 7,45%	i.v.	mmol/h	10
Calcium-Ion (gluconat)	i.v.	ml/h	10
KALIUMCHLORID 7,45% 1¶	i.v.	ml/h (mmol/h)	20 (10) 20 (10)
Natrium-Ion Hydrogencarbonat-Ion ¶	i.v.	mmol	50
Hydrocortison 50 mg/50ml (1 mg/ml) ¶	i.v.	mg	50
Rasburicase Rasburicase	i.v.	mg	1,5
SUFentanil 100 µg/50ml (2 µ¶	i.v. kont.	µg/kg/h	0,2 0,25
Midazolam 100 mg/50ml (2¶	i.v. kont.	mg/kg/h	0,2
Insulin 50 IE/50ml (1 IE/ml) ¶	i.v. kont.	I.E./kg/h	0,02 0,05 0,1 0,08
Glucose, wasserfrei zur parer¶	i.v. kont.	g/kg/d	5 4
NaCl 0,9% 50 ml für Nachlauf	i.v. kont.	ml/h	2 2
NaCl 0,9% 50 ml für Nachlauf	i.v. kont.	ml/h	2
Furosemid fUROsemid	i.v. Kurzinf.	mg	
Hydrocortison Hydrocortison	i.v. Kurzinf.	mg	20 20
Elektrolyt Inf. 1/1	Infusion	ml/h	400 400 200
Elektrolyt Inf. 1/1	Infusion	ml/h	60 60

Microbiology findings

Group A Streptococcus

- Pharyngeal swab

- Blood cultures (drawn after initiation of ABx) negative



Keim 1 geringes Wachstum von Sprosspilzen
Keim 2 reichliches Wachstum von Streptococcus pyogenes
Keim 3
Keim 4 geringes Wachstum von Staphylococcus aureus
Staphylococcus aureus:
PVL-Gen (Panton-Valentine-Leukozidin) negativ.
reichliches Wachstum von Keimen der Oropharyngealflora
Mäßiges Wachstum von Enterobacteriaceae

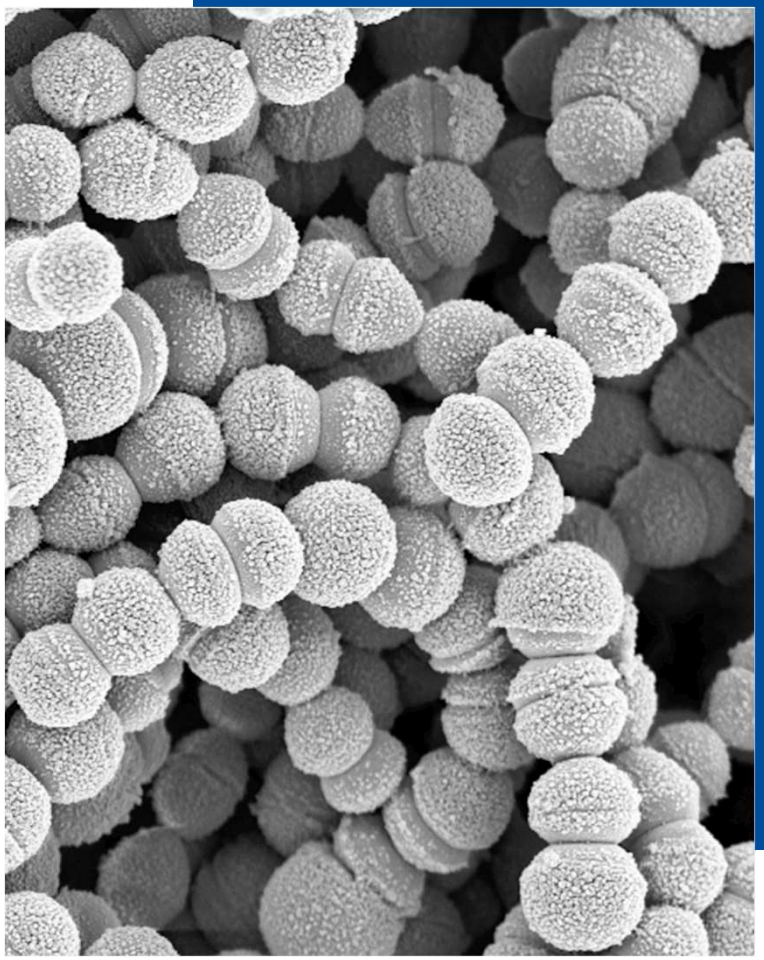
ANTIBIOGRAMM:	Keim 1	Keim 2	Keim 3	Keim 4	Keim 5	Keim 6
Keim 8						
Penicillin		S <=0.06		R >=0.5		
Ampicillin				R		
Oxacillin				S 0.5		
Cefoxitin-Screen				ne		
Ampicillin/Sulbactam				S		
Piperacillin				R		
Piperacillin/Tazobactam				S		
Cefazolin				S		
Cefuroxim				S		
Ceftriaxon				I		
Imipenem				S		
Meropenem				S		
Levofloxacin		I 0.5		R >=8.0		
Moxifloxacin		S 0.12				
Gentamicin		-		S <=0.5		
Tobramycin				S		
Teicoplanin		S <=0.12		S <=0.5		
Vancomycin		S <=0.12		S 1.0		
Induc.Clindamycin Resi		ne		ne		
Erythromycin		R >=8.0		R >=8.0		
Clindamycin		R >=1.0		S 0.25		
Tetracyclin		R >=16.0		S <=1.0		
Tigecyclin		S <=0.06		S <=0.12		
Linezolid		S <=2.0		S 2.0		
Chloramphenicol		-				
Daptomycin				S 0.5		
Fosfomycin				. <=8.0		
Fusidinsäure				S <=0.5		
Mupirocin				S <=1.0		
Rifampicin		S <=0.06		S <=0.03		
Cotrimoxazol		S <=10.0		S <=10.0		

Introduction

Introduction

Subtitle (optional)

- Group A Streptococci (GAS) are bacteria commonly causing mild infections like pharyngitis.
- However, they can lead to severe, invasive infections
- Rising incidence of invasive GAS infections makes this a public health concern



Streptococcus pyogenes
https://www.rki.de/DE/Themen/Infektionskrankheiten/Infektionskrankheiten-A-Z/S/Scharlach/Scharlach.html

Group A Streptococcus

- GAS lyses the red blood cells in the agar, resulting in clear colourless zones around the area of bacterial growth

- Lancefield classification: classifies catalase-negative gram-positive bacteria based on the carbohydrate composition of bacterial antigens found on their cell walls
- *Streptococcus pyogenes* is grouped as 'A' in the Lancefield system and is thus commonly called Group A *Streptococcus* (GAS)

Pathogenesis

Transmission

- GAS survival requires an unbroken cycle of transmission:
  → adherence to the primary infection site (skin or throat)
  →colonization and proliferation
  →defence against both innate and adaptive immune systems
  →subsequent dissemination to a new host
  →Incubation period 1-3 days (non invasive), or up to 30 days (iGAS)

Transmission

- New virulence strategies employed by GAS to manipulate host defence mechanisms are being discovered:

→ cleavage of Gasdermin A (GSDMA) by the GAS protease streptococcal pyrogenic exotoxin B (SpeB) has been shown to trigger host cell pyroptosis

→ mucosal-associated invariant T cells (MAIT cells) have been recently identified as highly activated in patients with STSS

→ primary contributors to the cytokine storm associated with this disease

Pathogenesis

Virulence Factor	Function	Associated Clinical Impact	Relevant Strains (Examples)
M Protein (*emm* types)	Inhibits phagocytosis, promotes adhesion	Linked to invasiveness, tissue tropism	*emm1*, *emm3*, *emm4*, *emm12*, *emm89* [6,14]
Streptolysin O (SLO)	Pore-forming cytotoxin damaging host cells	Beta-hemolysis, tissue injury	Broadly distributed [8]
Streptolysin S (SLS)	Cytolytic toxin contributing to hemolysis	Tissue damage, immune evasion	Broadly distributed [8]
Streptokinase	Converts plasminogen to plasmin, promotes fibrinolysis	Facilitates tissue invasion	Broadly distributed [8]
Hyaluronidase	Degrades connective tissue matrix	Promotes spread through tissues	Broadly distributed [8]
SpeB (cysteine protease)	Degrades host proteins and immune mediators	Modulates immune response, promotes tissue destruction	Various *emm* types [8]
Pyrogenic Exotoxins (SpeA, SpeC, etc.)	Superantigen activity leading to massive cytokine release	Linked to STSS, severe invasive disease	SpeA, SpeC in *emm1*, *emm3*, *M1UK* [9,10,11,12,13]

STSS: Streptococcal toxic shock syndrome.

Clinical manifestation

Clinical Manifestations

overview

- Asymptomatic colonization!
- invasive and non-invasive infections of varying severity
- may be accompanied by toxin-mediated disease such as
  - → streptococcal toxic shock syndrome (STSS)
  - → scarlet fever
- post-infectious immune sequelae such as
  - → acute rheumatic fever
  - → rheumatic heart disease
  - → post-streptococcal glomerulonephritis

Clinical Manifestations

Invasive disease

- Necrotizing fasciitis with deep tissue destruction; surgical emergency
- Cellulitis: rapidly spreading erythema, edema, pain
- Myositis: rare but serious
- Streptococcal toxic shock syndrome (STSS)
  - → Hypotension, multiorgan failure, rash, coagulopathy
- Bacteremia, and sepsis
  - → Seeding distant sites
- Meningitis
- Pneumonia
  - → often with empyema or pleural effusion.

Clinical Signs

Invasive disease

- High fever
- Shivering
- Headache
- Respiratory distress
- severe pain in arms or legs
- sore throat
- red or sore skin around cuts or wounds
- abdominal pain

Treatment

- No resistance against ß-lactam ABx known in the past

- Non-invasive disease:

  → Penicillin or amoxicillin 10 days (5 days?)

  → Alternative in children: Oral cephalosporines (e.g. cefaclor)

  → Allergies: oral macrolides (e.g. erythromycin, azithromycin) 10-30% resistance rates

  → Cotrimoxyzol and flourochinolones generally *not* effective

- **Invasive disease:**

  → **Penicillin i.v. + Clindamycin + immunoglobulin**

Resistance

Esposito et al. Microorganisms 2025, 13(8), 1871

Region/ Country	Antibiotic	Resistance Rate (%)	Associated *emm* Types/Notes
Taiwan	Macrolides	18.1% (2000–2009) → 58.4–61.6% (2010–2019)	Predominantly *emm12* strains [40]
China	Macrolides	~97.5%	High resistance among both patients and carriers
China	Clindamycin	~97.3%	Significant resistance documented
China	Tetracyclines	~95.7%	Notable regional variability
Australia	Tetracyclines	~10%	Lower resistance rates observed
China	Tetracyclines	>80%	Substantially higher than global averages
Hungary	Quinolones	~10%	Notable but relatively low resistance overall
Japan	Quinolones	~14%	Emerging resistance trend

Epidemiology

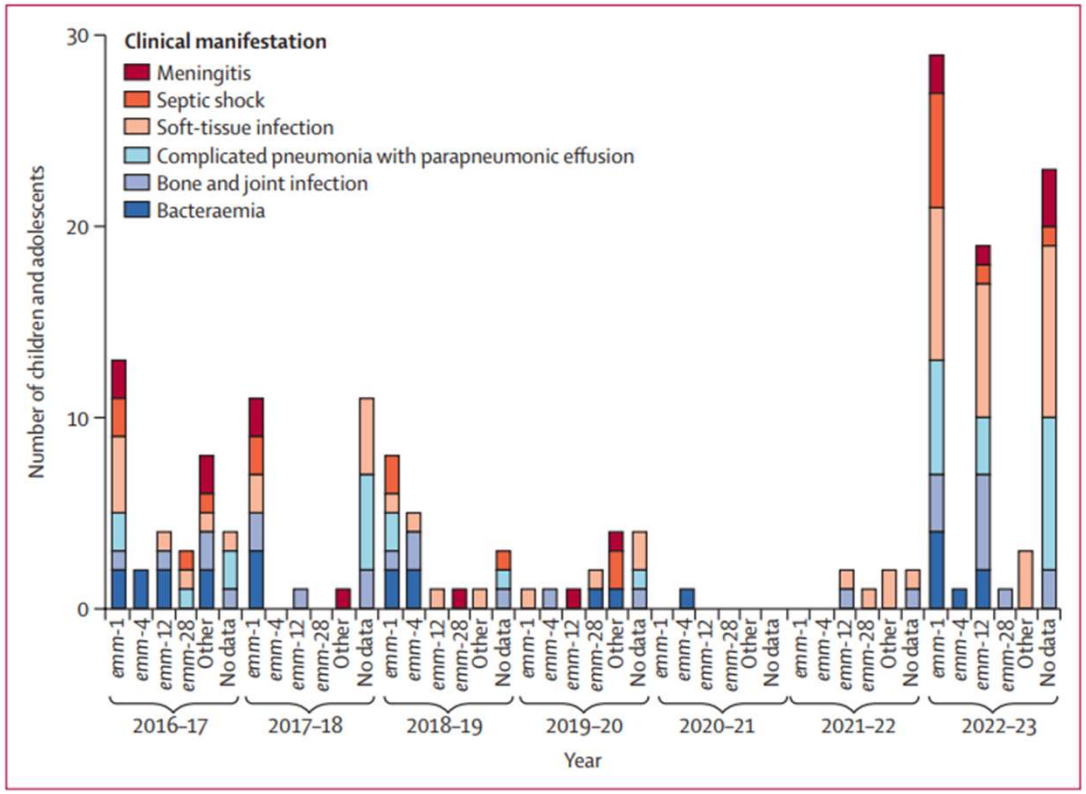
Epidemiology

Subtitle (optional)

- GAS can be classified into more than 220 *emm* types (based on the gene sequence of the amino terminal of the surface-exposed M protein)
- different patterns of regional and global distribution
- Increasing global and regional incidence of invasive GAS since 2019
- Surges in winter seasons and post-COVID periods
- Higher risk in children, elderly, and immunocompromised individuals

Epidemiology

Nygaard et al., Lancet Child Adolesc Health 2024; 8: 112–21



	Paediatric intensive care unit			Mortality	
	Before 2022–23	2022–2023	p value*	Before 2022–23	2022–2023
Phenotypes	17	17	..	3	3
Non-focal bacteraemia	0/18 (0%)	0/7 (0%)	1·00	0/18 (0%)	0/7 (0%)
Bone and joint infection	0/18 (0%)	0/11 (0%)	1·00	0/18 (0%)	0/11 (0%)
Soft-tissue infection†	3/27 (11%)	7/27 (26%)	0·29	0/27 (0%)	1/27 (4%)
Complicated pneumonia with parapneumonic effusion	4/14 (29%)	1/17 (6%)	0·15	0/14 (0%)	0/17 (0%)
Septic shock	5/11 (46%)	6/8 (75%)	0·35	1/11 (9%)	2/8 (25%)
Meningitis	5/10 (50%)	3/6 (50%)	1·00	2/10 (20%)	0/6 (0%)
emm variants	17	17	..	3	3
emm-1	10/33 (30%)	9/29 (31%)	0·53	2/33 (6%)	2/29 (7%)
emm-12	1/9 (11%)	2/19 (11%)	1·00	0/9 (0%)	0/19 (0%)
emm-28	1/7 (14%)	0/1 (0%)	1·00	1/7 (14%)	0/1 (0%)
emm-4	1/9 (11%)	0/1 (0%)	1·00	0/9 (0%)	0/1 (0%)
Other variants	1/16 (6%)	0/3 (0%)	1·00	0/16 (0%)	0/3 (0%)
Not available	3/24 (13%)	6/23 (26%)	0·49	0/24 (0%)	1/23 (4%)

Data are n, n/N (%), or p value. Denominators are the total number of children and adolescents with each phenotype or *emm* variant who were either admitted or not admitted to PICU. *p values were derived from Fisher's exact test—except for soft tissue and *emm*-1, which were derived from Pearson's χ^2. †Five (19%) of 27 children with soft-tissue infections had necrotising fasciitis in 2022–23 *vs* one (4%) of 27 in 2016–17 to 2021–22 (p=0·19).

***Table 3*: Danish children and adolescents with invasive group A streptococcal disease who received treatment at a paediatric intensive care unit or died in 2022–23 *vs* 2016–17, 2017–18, 2018–19, 2019–20, 2020–21, and 2021–22**

Epidemiology

Nygaard et al., Lancet Child Adolesc Health 2024; 8: 112–21

- historically low iGAS incidence during the COVID-19 pandemic
- 4-fold increase in complicated pneumonia with parapneumonic effusion
- 4·5-fold increase in severe soft-tissue infections
- GAS resurgence in 2022–23 was associated with reduced immunity to GAS due to historically low GAS and iGAS incidences during the COVID-19 pandemic
- the resurgence might have been influenced by the increase in viral infections after the COVID-19 pandemic
- high morbidity of iGAS highlight iGAS as a major invasive bacterial infection in children, surpassing meningococcal disease in Denmark.

Risk factors

Nygaard et al., Lancet Child Adolesc Health 2024; 8: 112–21

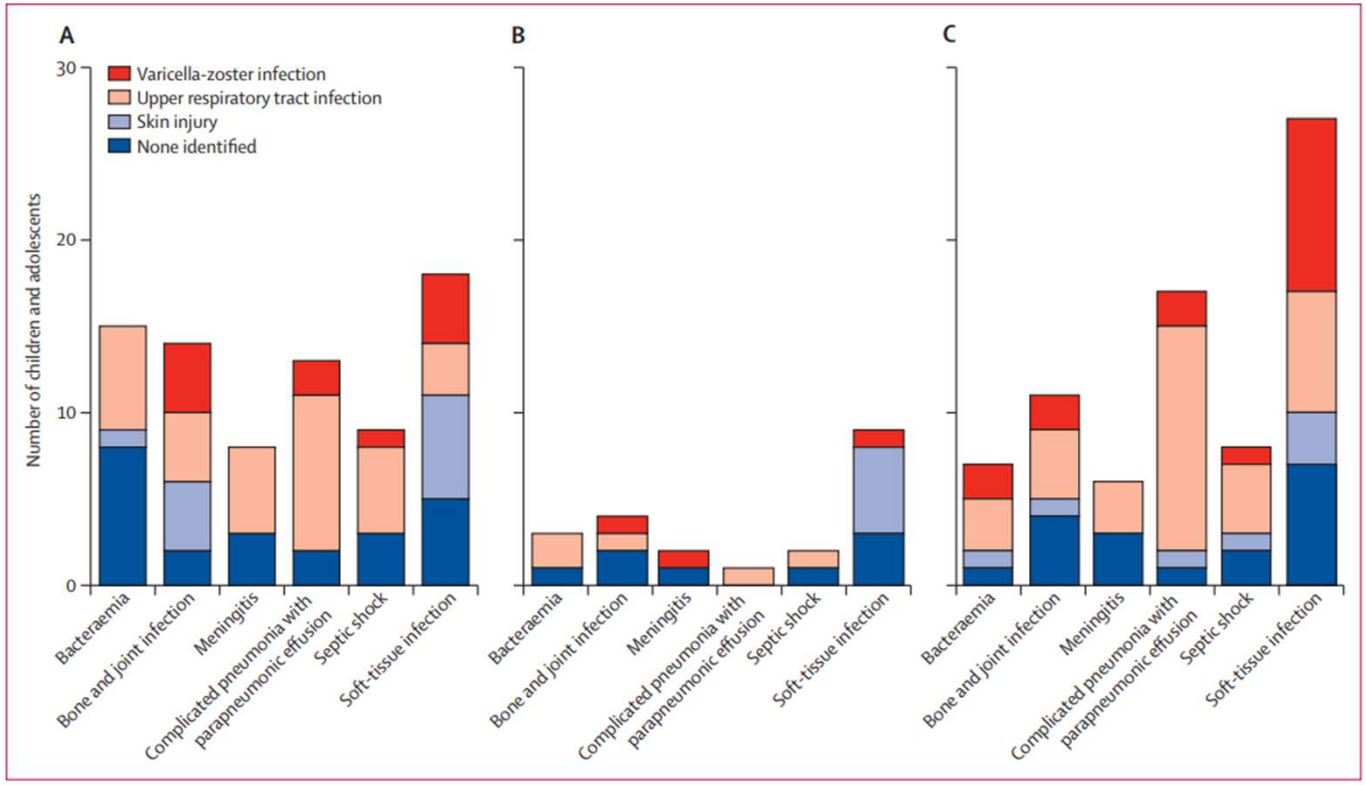
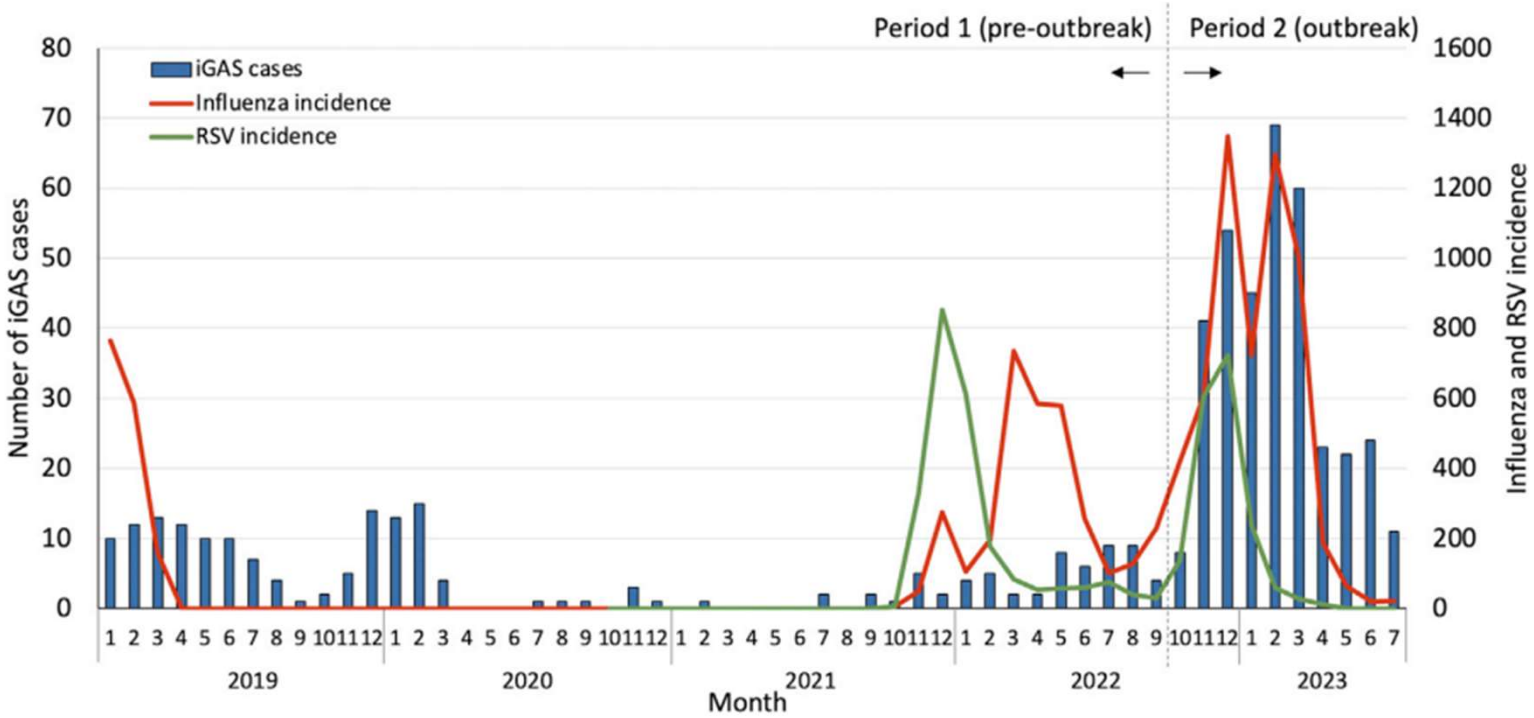


Figure 3: **Predisposing conditions for each distinct phenotype of invasive group A streptococcal disease in children and adolescents in Denmark**
(A) 2016–17, 2017–18, and 2018–19. (B) 2019–20, 2020–21, and 2021–22. (C) 2022–23.

Severity of cases

Cobo-Vázquez et al., International Journal of Infectious Diseases, 2025; 159.



Severity of cases

Cobo-Vázquez et al., International Journal of Infectious Diseases, 2025; 159.

- higher PICU admissions (51.3% vs. 30.8%, P < 0.001)

- Pneumonia was the most common syndrome (32.3%)

  → with pleural effusion in 58.3%

- most frequent emm1 (56.1%) (increased ICU-rates) and emm12 (27.1%)

Severity of cases

Cobo-Vázquez et al., International Journal of Infectious Diseases, 2025; 159.

- Factors associated with PICU were
  - → streptococcal toxic shock syndrome (STSS)
  - → Pneumonia
  - → necrotizing fasciitis
  - → acute kidney failure
  - → previous consultation before diagnosis
- Mortality: 2% (n=11)
- Factors associated:
  - → Sepsis
  - → STSS
  - → central nervous system infection

Recent Surge in Cases

- Reports from CDC, ECDC, and other national bodies
- Marked increase in cases post-2022

- Possible reasons: reduced immunity post-pandemic, viral co-infections
- super antigens: introduced after infection by phages
- Facilitate mucosal colonization and immuno-evasion (e.g. neutrophil killing by DNAse)

Outlook

Prevention

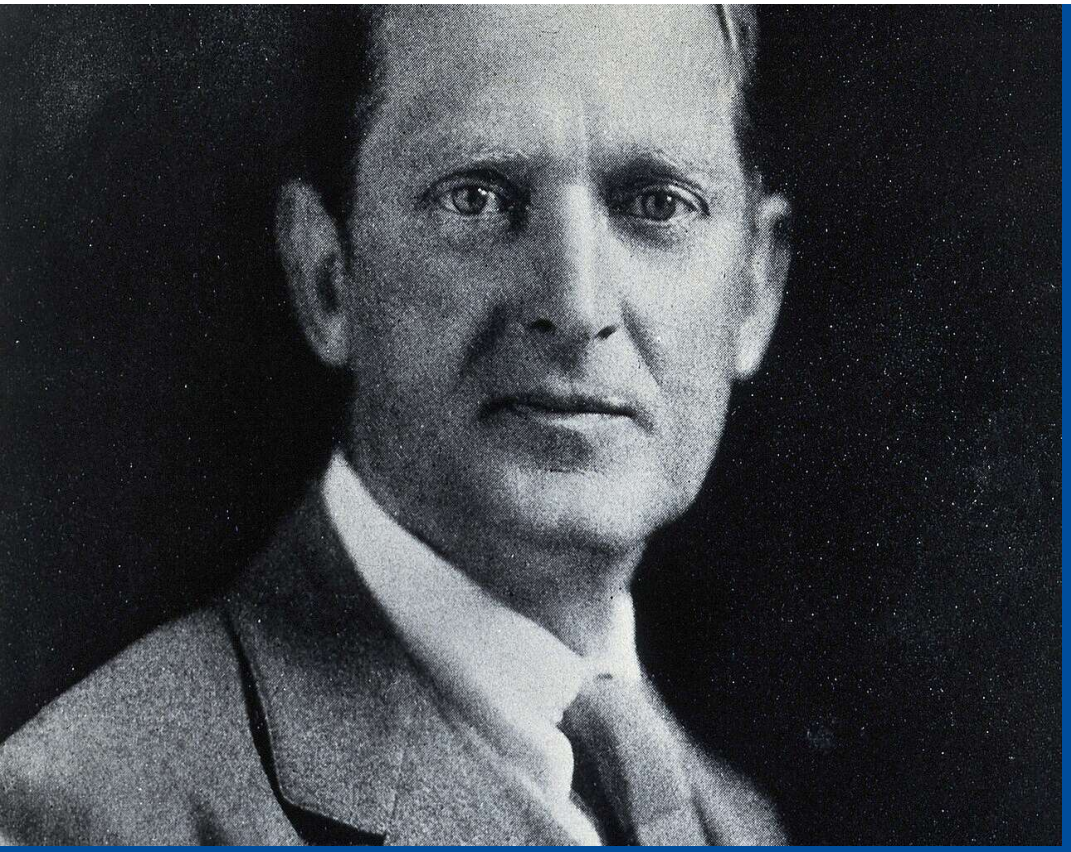
- GAS-Vaccines:
  - → Several attempts – from 1920 to our day and age
  - → No breakthrough
- Varicella immunization may reduce iGAS incidence in children
- Education (ABS, AMR)
- Hygiene measures
  - → Very susceptible to general disinfectants
  - → Quarantine 24h
  - → No special measures for contacts
  - → Sepsis/STSS/necrotizing fasciitis: Chemoprophylaxis for close contacts
- Early treatment of mild streptococcal infections

Future developments

Esposito et al. Microorganisms 2025, 13(8), 1871

- novel antimicrobial approaches as adjuncts or alternatives to conventional antibiotics.
  - →bacteriophage-derived lysins with specific lytic activity against GAS
  - →engineered antimicrobial peptides with broad-spectrum efficacy
  - →anti-virulence compounds targeting toxin production
  - →particularly relevant for managing life-threatening iGAS infections

- Continued research and investment necessary



"

Infectious Disease is one of the few genuine adventures left in the world.

Hans Zinsser (1878-1940), "Rats, Lice an History"